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APPLICATION OF PALLADIUM NANOPARTICLES IN THE REDUCTION OF ORGANIC FUNCTIONAL GROUPS

By

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ABSTRACT

APPLICATION OF PALLADIUM NANOPARTICLES IN THE REDUCTION OF ORGANIC FUNCTIONAL GROUPS

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 fluoride activated polymethylhydrosiloxane (PMHS) was developed. A desire to modify the system to include aromatic chlorides, led to the finding that PMHS reacts with $Pd(OAc)_2$ to form palladium nanoparticles, which in combination with PMHS and aqueous KF will rapidly hydrodehalogenate aryl chlorides at room temperature. Through substrate screening in the chlorodehalogenation system it was found that the palladium-PMHS nanoparticles in combination with an aromatic chloride promote the chemo-, regio-, and stereoselective reductive cleavage of benzylic C-O bonds. It was also determined that $Pd(OAc)_2$/PMHS/KF system can efficiently reduce aromatic nitro groups to amines, and aliphatic nitro groups to *N*-hydroxylamines by modifying the system to $Pd(OAc)_2/Et_3SiH$. The slight Lewis acidity of the palladium nanoparticles was also capitalized upon to perform a one-pot reductive transformation of the aromatic nitro groups to amides, sulfonamides, and carbamates.

To Jill and my father

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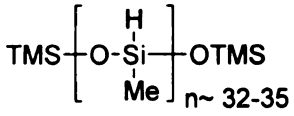
LIST OF ABBREVIATIONS

Ac	acetyl
acac	acetylacetonate
AIBN	2,2'-azobisisobutyronitrile
aq	aqueous
CCl_4	carbon tetrachloride
CH_2Cl_2	dichloromethane
$Cl_2Pd(PPh_3)_2$	dichlorobis(triphenylphosphine)palladium(II)
dba	dibenzylideneacetone
DMF	N,N-dimethylformamide
DMSO	dimethyl sulfoxide
equiv	equivalent
EtOAc	ethyl acetate
Et_3SiH	triethylsilane
g	gram
h	hour
KF	potassium fluoride
LAH	lithium aluminum hydride
m	minutes
M	molar
mL	milliliter
mmol	millimole
$Pd(OAc)_2$	palladium(II) acetate

Ph	phenyl
PhCl	chlorobenzene
PhEt	ethylbenzene
PMHS	polymethylhydrosiloxane
r.b.	round bottom
r.t.	room temperature
R.T.	retention time
S.M.	starting material
THF	Tetrahydrofuran
TMS	Trimethylsilyl

Chapter 1. The Evolution of PMHS in Organic Chemistry



Polymethylhydrosiloxane (**PMHS**)

A growing theme in organic chemistry is the development of reagents that are environmentally friendly, inexpensive, and readily available. An avenue which automatically meets some of these criteria that has not been fully explored to it's potential, is exploring the utilization of industrial byproducts in organic synthesis. Polymethylhydrosiloxane (PMHS) is one such reagent, being a byproduct of the silicon industry's synthesis of cyclicsiloxanes. PMHS is inexpensive, approximately $7.2 per mol of hydride, and readably available from a number of distributors. It is air and moisture stable, can be stored on the bench for years at a time with no detrimental effect, is environmentally benign, and is assumed to be non-toxic.

Polymethylhydrosiloxane (PMHS)[1] was first synthesized in 1946 by Sauer,[2] and has been available for over fifty years. Despite this fact, PMHS has seen limited use, especially when compared to other silicon hydride reagents, such triethylsilane.[3] Over the past 15 years the use of PMHS has grown, which may be attributed to it's tolerance of most organic functionality, the ability to transfer it's hydride to a variety of transition metals, and the other favorable characteristics stated above. From 1960 to 1992 there were less than 10 publications and patients reported per year using PMHS. Starting in 1993 the number of publications and patients began to dramatically increase with over 150 articles and patents submitted in 2005 alone.

PMHS by it self is typically incapable of reducing organic functionality, but in combination with a fluoride source PMHS can reduce aldehydes, ketones, and esters to alcohols; and α,β-unsaturated carbonyls undergo 1,2 and 1,4 reduction with poor selectivity. The asymmetric reduction of ketones has been achieved with chiral ammonium fluoride salts. Activation of PMHS for reduction of carbonyls has also been accomplished with non-fluoride sources, such as Triton B®. PMHS ability to transfer its hydride to a metal has been it's most frequent application in organic synthesis. It has been used with Al, Co, Cr, Cu, Fe, In, Mn, Ni, Pd, Rh, Ru, Sn, Ti, Zn, and Zr to promote a verity of reactions from hydrometallation of alkynes to the reduction, or asymmetric reduction, of carbonyls, esters, lactones, imines, alkenes, alkynes, and nitrobenzene.

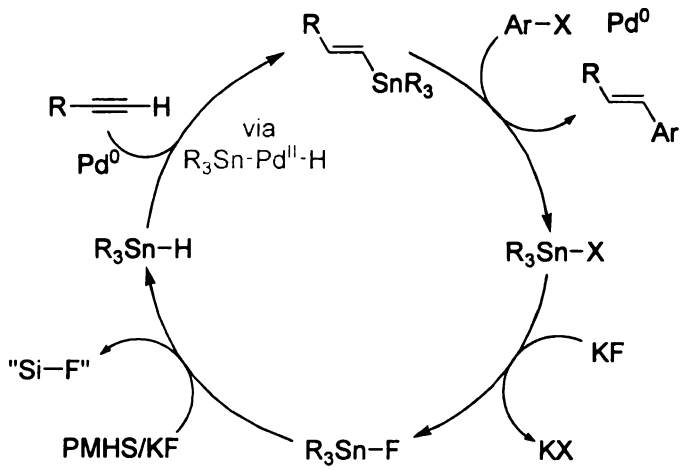
Chapter 2. $Cl_2Pd(PPh_3)_2$ Catalyzed Dehalogenation of Iodo- and Bromoarenes via Fluoride Activated PMHS

2.1 Introduction

One of the better-known applications of PMHS is in the synthesis of trialkyltin hydrides; first accomplished by Hayashi from the corresponding tin oxide species.[4] Attempts to extend Hayashi's method, to organotin halides as the tin hydride precursors could not be accomplished. The Maleczka group theorized that fluoride activation of PMHS could allow for a more facile hydride transfer, through formation of a polycoordiante silicon hydride, and thereby convert trialkyltin halides to trialkyltin hydrides. Maleczka and Terstiege demonstrated that the combination of PMHS and aqueous potassium fluoride, in an ethereal solution, efficiently synthesized tributyltin hydride from the corresponding tributyltin chloride, proving their theory correct. The in situ generation and reaction of trialkyltin hydride in subsequent chemical transformations was then investigated. It was found that 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 triorganotin halide byproduct.[5] Maleczka and co-workers followed this work with the in situ preparation of vinylstannanes from the organotin halides, under palladium catalysis and free radical conditions.[6] With these results in hand the PMHS, aqueous KF, catalytic Bu_3SnCl combination was successfully applied to a one-pot palladium catalyzed hydrostannation / Stille coupling.[7] Originating from the

envisioned mechanistic cycle shown in Scheme 1. One of the potential problems that was foreseen in the developing stages of this protocol, was that in-place of transmetallation of the vinylstannane with the organopalladium (II) halide species, hydride transfer may be favored, resulting in reduction of the halogen electrophile. Fortunately, this was found to be an unwarranted concern. As such, a question arose from this positive result, could fluoride activation of PMHS promote a palladium catalyzed hydrodehalogenation?

Scheme 1. Proposed Catalytic Cycle for a One-Pot Hydrostannation/Stille Coupling



2.2 General Aspects of Dehalogenations

There are three reasons for developing and/or using dehalogenation methodology: (1) For the degradation of hazardous materials, such as PCB's, PBB's, pesticides, etc;[8,9] (2) For deuterium labeling of organic compounds that are to be use in mechanistic studies;[10] (3) For the removal of halogen(s) that are used as directing or protective groups in organic synthesis.[11] A plethora of reagents and systems have been developed for universal or reaction specific dehalogenations, the majority of which follow the general order I > Br > Cl >> F

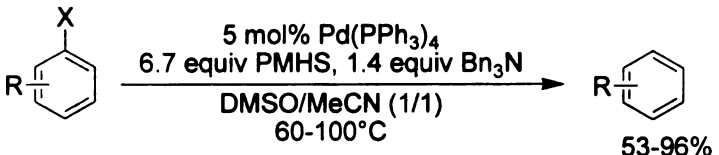
for ease of dehalogenation. The dissociation energy of carbon-halogen bonds (C-I, 53 kcal/mol; C-Br, 67 kcal/mol; C-Cl, 81 kcal/mol; C-F, 109 kcal/mol) can be used as a rough guide to explain the order of dehalogenation. Indeed it is possible to perform selective hydrodehalogenations of specific halides. 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,[12,13] oxidative,[14] metal catalyzed hydride delivery,[12,15,16,17,18,19] and also under free radical conditions[12,20] are among the common ways to perform such hydrodehalogenations.

2.3 $Cl_2Pd(PPh_3)_2$ Mediated Reductions of Iodo and Bromoarenes

Of the vast number of methods developed for dehalogenation there still remains room for improvement in terms of shorter reaction times, the use of environmentally friendly reagents, ease of purification, and the ability to scale up. One reagent that is capable of meeting these requirements is PMHS. In 1986, Pri-Bar and Buchman[16b] reported that PMHS in the presence of a Pd(0) catalyst could effectively reduce aryl, styryl, and α-keto bromides and iodides (Scheme 2). 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 $Pd(PPh_3)_4$. Given the aforementioned fluoride activation of PMHS,[5,21] it was decided to investigate if a combination of PMHS and fluoride would facilitate

aryl halide reductions and thereby minimize some of the disadvantages posed by the original protocol.

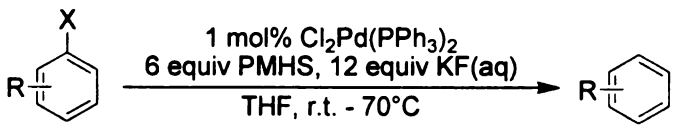
Scheme 2. Pri-Bar and Buchman System



X = I and Br
R = Ar, Cl, C(O)R', CHO, CO_2H, NO_2, styryl, a-keto

Screening various catalysts, solvents, fluoride sources, stoichiometries, and reaction temperature combinations revealed that like the original conditions ~6 equiv. of PMHS worked best (Scheme 3).[16a] 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% while simultaneously switching to a more stable palladium source, and facilitated the reduction in a more user friendly solvent, THF, at 70°C or lower (Table 1). Control experiments clearly identify the fluoride additive promoting the reduction, for dehalogenation's run in the absence of KF saw yields diminish by ~80% for the aryl bromides to ~30% for the aryl iodides.[22]

Scheme 3. $Cl_2Pd(PPh_3)_2$\PMHS\KF(aq) Dehalogenation System



X = I and Br

As compared to the hydrodehalogenations described by Pri-Bar and Buchman, reductions under the $Cl_2Pd(PPh_3)_2$\PMHS\KF conditions tended to be higher yielding, though at the cost of longer reaction times, which can be

attributed to the lower catalysts concentration.[23] Despite this increased reaction time, by avoiding the amine and high boiling polar solvents, reaction monitoring (GC and NMR) as well as product isolation and purification were simplified. 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.

The results of the $Cl_2Pd(PPh_3)_2$ catalyzed hydrodehalogenation experiments can be found detailed in Table 1, where it was determined that iodobenzene is efficiently reduced to benzene at room temperature, and simply heating the reaction to 70 °C decreases the reaction time by half (entries 1-2). This was not the case for bromobenzene, which required heating at 70 °C for complete reduction (entry 3). Judicious selection of the reaction temperature allowed selective reduction of an iodide in the presence of a bromide, and a bromide in the presence of a chloride (entries 4-5). In the process of reducing the mixed dihalides, it was observed that Pd black precipitated out of solution after reduction of the more facile halide. The system tolerated a variety of electron withdrawing functional groups (nitro, aldehyde, ketone, ester), smoothly dehalogenating an iodided or bromide in good to near quantitative yields (entries 6-10). The system is not limited to haloarenes, α-bromo-carbonyl compounds (entries 11-12) can also be reduced, albeit with minor side product formation.[24]

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 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).

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

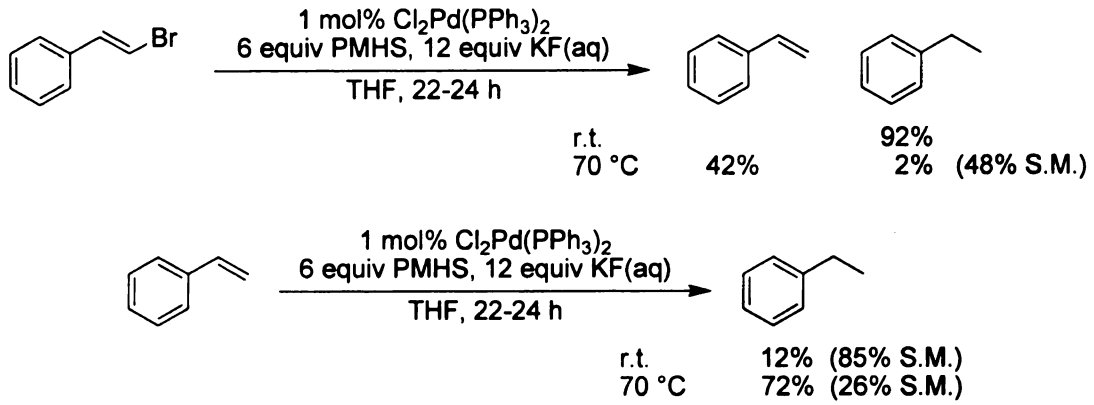
Entry	Starting Material	Temp. (°C)	Time (h)	Product	% Yield[b]
1	Iodobenzene	r.t.	24	Benzene	90[c]
2	Iodobenzene	70	11	Benzene	100[c]
3	Bromobenzene	70	36	Benzene	100[c]
4	1-Bromo-4-iodobenzene	r.t.	26	Bromobenzene	100
5	3-Bromochlorobenzene	70	48	Chlorobenzene	90
6	1-Bromo-4-nitrobenzene	70	3.5	Nitrobenzene	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: Aromatic halide (1 mmol), $Cl_2Pd(PPh_3)_2$ (0.01 mmol), KF (12 mmol), PMHS (6 mmol), 5 mL THF, and 2 mL 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

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 11). 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 transfer hydrogenation with PMHS has been described.[25] 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).

Scheme 4. Conflicting Results of β-Bromostyrene and Styrene



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). Monitoring the reduction of β-bromostyrene by GC, for the room temperature and 70 °C reaction, confirmed that β-bromostyrene reduces first to styrene and then on to PhEt. This result makes the interpretation of the data more difficult, for 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 subtle difference between the two substrates, a halide. 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.

These results prompted us to repeat[26] 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 13).[27] No PhEt was observed when styrene was subjected to these conditions (entry 14), suggesting again an involvement of the halide in the over reduction.

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

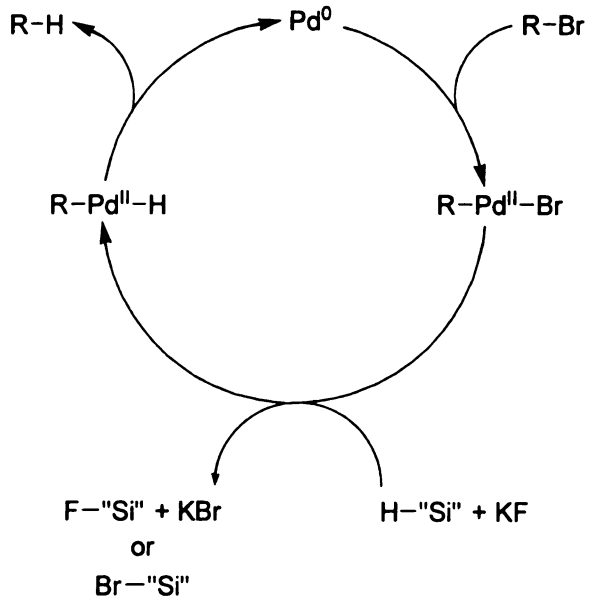
Entry	Starting Material	Temp (°C)	Time (h)	Product	% Yield[b]
1	β-Bromostyrene	r.t.	24	PhEt	92[c]
2	β-Bromostyrene	70	22	Styrene	42[c]
3	Styrene	r.t.	24	PhEt	12[c,d]
4	Styrene	70	24	PhEt	72[c,d]
5	Styrene + KBr	r.t.	24	PhEt	12[c,d]
6	Styrene + TMSBr	r.t.	24	--	--
7	β-Bromostyrene + Proton-Sponge	r.t.	24	PhEt	92[d]
8	Styrene + 2-Bromoacetophenone (1/1)	r.t.	24	PhEt	78[d]
9	Styrene + 2-Bromoacetophenone (1/1)	70	22	PhEt	43[d]
10	1 equiv Styrene + 0.2 equiv 2-Bromoacetophenone	r.t.	24	PhEt	27[d]
11	Styrene + Bromobenzene (1/1)	r.t.	24	PhEt	64[d]
	Under Pri-Bar and Buchman's Conditions				
12	β-Bromostyrene	60	3	Styrene	37[e]
13	β-Bromostyrene	60	3	PhEt	25[d,f]
14	Styrene	60	3	No rxn	-

a) Conditions: Starting material (1 mmol), $Cl_2Pd(PPh_3)_2$ (0.01 eq.), KF (12 eq.), PMHS (6 eq.), 5 mL THF, and 2 mL H_2O b) Yields are the average of two runs c) As determined by GC (calibration curve) d) As determined by NMR (internal standard) e) Per Ref. 16b f) Our data

Contemplation about the role of the halide started with rationalizing the mechanism of reduction of the organic halide, followed by surmising the ultimate fate of the halide. Drawing on past literature precedent, a catalytic cycle of oxidative addition, hydride transfer, reductive elimination (Scheme 5) is likely operative for the reduction. Per such a mechanism there are two possible fates

for the halide in the hydride transfer step, formation of KBr, or formation of a silicon bromide, which under the aqueous conditions could be hydrolyzed to HBr. To evaluate if KBr or HBr is facilitating the facile reduction of the olefin at room temperature a number of control reactions were conducted. First, styrene was subjected to the reaction conditions with 1 equivalent of KBr (entry 5), which failed to promote the reduction.[28,29] At this point, 1 equivalent of bromotrimethylsilane was used as the additive in the reduction of styrene (entry 6), resulting in the complete polymerization of styrene, discounting the olefin reduction being facilitated by HBr. To fully eliminate HBr as the promoter of the over reduction, β-bromostyrene was resubjected to the reaction conditions in the presence of 1 equivalent of Proton-Sponge®, where ethyl benzene was afforded in near quantitative yield (entry 7).

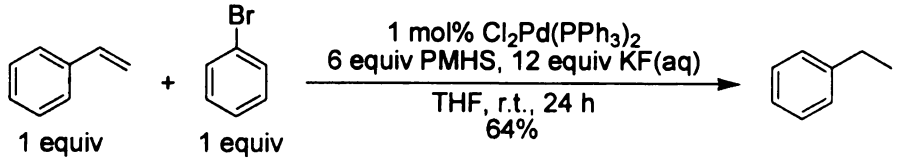
Scheme 5. Proposed Catalytic Cycle for Reduction of the Organic Halide



Having dismissed KBr and HBr as the promoters of the over reduction, examination into an organo palladium(II) bromide species catalyzing the

reduction was investigated. To test this it was felt that an organic bromide could simply be added to the reduction of styrene. 2-Bromoacetophenone was chosen for this role as it had already been determined that this substrate could be reduced at room temperature and 70 °C under the reaction conditions. Room temperature reduction of a 1/1 mixture of styrene and 2-bromoacetophenone afforded a 78% yield of PhEt after 24 h (entry 8). 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 9). Decreasing the amount of added 2-bromoacetophenone met with a corresponding decrease in the yield of PhEt (entry 10). To substantiate the results of 2-bromoacetophenone, styrene was resubjected to the reaction conditions at room temperature with bromobenzene, affording PhEt in 64% (Scheme 6). So while the results indicate that a organopalladium(II) bromide plays a role, the specifics of the mechanism by which the alkene is saturated remain unclear.[30] The decreased yield when run at 70 °C might also be explained by in situ formation of a unique palladium(II) catalyst that is thermally unstable. Evidence of this possibility being the observation of palladium precipitation under the thermal conditions.

Scheme 6. Facilitating the Facile Reduction of Styrene with Bromobenzene



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.

Chapter 3. Discovery and Application of Palladium Nanoparticles in Chloroarene Dehalogenation

3.1 Palladium Nanoparticles in Organic Synthesis

The development of transition metal catalysts that promote new reaction pathways, allow known pathways to be run with lower catalyst concentrations, the ability to recycle the catalyst with no loss in activity, or catalyze a reaction under aqueous condition and/or open to the air, is an on going endeavor. The development of nanostructured transition metals is one area of research that is attempting to address these issues. This field of research has been around since the late 1800's. In fact the most utilized method for the generation of zerovalent metal colloids developed in 1857 by M. Faraday, where a transition metal salt is reduced in the presence of a stabilizing agent in an organic or aqueous solvent. Metal colloids are metal particles that range in size from 1 to 100 nm. They are typically composed of a suspension of a solid or liquid phase distributed throughout a second phase in such a way that the particles do not settle out, or undergo spontaneous deposition. Metal colloids need to be stabilized to inhibit agglomeration, which is typically accomplished through electrostatic or steric stabilization. Advancements in the synthesis of metal colloids, and imaging technology have expanded the definition of "nano" materials to include nanopowders, nanoparticles, and nanoclusters. Nanopowders are characterized only by their size and elemental composition, with a large size distribution between 5-50nm, and the metal particles may or may not be aggregated. Nanoparticles are protected against agglomeration through electrostatic or steric

stabilization, and have a small size distribution between 1-10nm. The properties of the nanoparticle can vary by size, for the size of the nanoparticle is an inverse representation of the percentage of metal atoms at the surface. "Thus, a nanoparticle of 10nm diameter has about 10% of its atoms in the surface, but one of 1 nm has 100%."[31] Nanoclusters differ in that a known number of atoms occupy a specified amount of space, 1-15nm, and in specific cases having a defined chemical formulae.

A large variety of transition metal colloids have been synthesized, and their physical properties studied.[32] Despite the large volume of work that has been conducted in the preparation and study of metal colloids, application of these metal colloids in organic synthesis has been limited.[31,32d,33] Of the transition metal colloids, palladium colloids, nanoparticles, and nanoclusters are the most widely developed for catalyzing organic reactions.[31,34] The potential advantages of palladium colloids in organic synthesis (milder reaction conditions, lower catalyst concentrations, recycling of the catalyst, air and/or moisture stable catalysts) has driven their application in Heck,[35] Suzuki,[36] Stille,[37] Sonogashira,[38] Tsuji-Trost[39] reactions, oxidations,[40] carbonylations,[41] and hydrogenations.[42] The development and application of palladium colloids to this point has demonstrated the potential and utility of these catalysts, but the field remains in its infancy.

3.2 Discovery and Development of a Palladium Catalyzed Hydrodehalogenation of Chloroarenes

The $Cl_2Pd(PPh_3)_2$/PMHS/KF dehalogenation system described in Chapter 2 was unable to reduce aromatic chlorides; this can be advantageous as it allows

chlorides to be used as directing or protective groups. Moreover, a vast number of organic chlorides are commercially available, inexpensive, and extremely stable. However, if after serving in such a role the chloride is to be removed then modification of the original system to include aromatic chlorides would be beneficial. Thus the development of a method to transform these chlorinated compounds is of great interest.

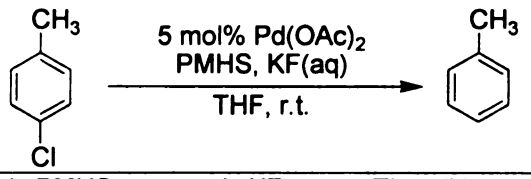
Silicon hydrides have precedent in reducing carbon chlorine bonds, PMHS has been demonstrated to reduce polychlorinated biphenyl's (PCB's) with sodium or lithium metal,[43] and a combination of triethylsilane and palladium chloride can reduce aliphatic and aromatic chlorides at room temperature.[44] Along these lines, silicon hydrides have also been shown to react with transition metals to form more reactive catalysts. Crabtree and co-workers found that PMHS reacts with $Pd(hfacac)_2$ to form Pd(0)-colloids, which can reduce enones, alkynes, a nitro group, and an acid chloride under hydrogen gas, or with triethylsilane.[45] Tour and co-workers found that $(EtO)_3SiH$ reacts with $Pd(OAc)_2$ in a THF/H_2O mixture to form finely divided palladium on a polysiloxane matrix, which was an active catalyst for the reduction of enones, mono-substituted olefins, alkynes to alkenes, and alkynes to the fully saturated product.[46] Based on these facts, the supposition that simply changing the palladium source to a palladium salt, in conjunction with fluoride activated PMHS, would allow for the hydrodehalogenation of aromatic chlorides through the formation of a more active catalyst, a palladium colloid.

The first experiment designed to test this hypothesis was subjection of chlorobenzene to the initial dehalogenation conditions, but $Pd(OAc)_2$ would be used in place of $Cl_2Pd(PPh_3)_2$. The reaction was set up in sealed tube, and per the original procedure PMHS was added last, with no concern over the rate of addition. Upon injection of the PMHS, the reaction mixture immediately turned black, then erupted out of the sealed tube prior to capping. Examination of the remaining reaction mixture by NMR, clearly showed the chlorobenzene had reduced to benzene, thereby proving the hypothesis correct and warranting further investigation. The impressive transformation of chlorobenzene to benzene at room temperature in a matter of minutes was attributed to the formation of a palladium colloid, from $Pd(OAc)_2$ and PMHS, per the analogous results of Crabtree and Tour. To lay creed to the formation of a palladium colloid as the newly formed more reactive catalyst, $Pd(OAc)_2$ was dissolved in THF followed by the slow dropwise addition of PMHS. This caused the orange solution to turn dark brown and then produce clumps of a black sponge-like solid. Chlorobenzene was then subjected to the reaction conditions using the black sponge solid to catalyze the reduction. Again this resulted in the formation of benzene. Chauhan later confirmed our belief that the sponge-like material, formed when $Pd(OAc)_2$ reacts with PMHS, is in fact comprised of palladium nanoparticles of approximately 3.5 nm in size.[47]

With the structural nature of the catalyst at least partially defined we next sought to optimize and better understand the dechlorination reaction itself. 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 5-8). The use of 2 eq. KF with an excess of PMHS (6 eq.) produced the largest percent conversion (entry 3), so optimization of the PMHS concentration was performed using 2 eq. KF (Table 3, entries 9-14). As for the amount of PMHS required, increasing the equivalency of PMHS increased the rate of dehalogenation. For all of the PMHS concentrations tested, 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

Table 3. Optimization of KF and PMHS Concentrations[a]



Entry	equiv PMHS	equiv KF	Time (h)	% Conversion[b]
1	6	0	24	Trace
2	6	1	2	77
3	6	2	2	95
4	6	4	2	59
5	6	6	2	40
6	6	8	2	34
7	6	10	2	43
8	6	12	2	41
9	1	2	2.5	43
10	2	2	2	75
11	3	2	2	73
12	4	2	2	85
13	5	2	2	90
14	6	2	2	95

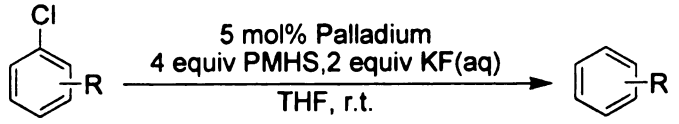
a) Performed on 1 mmol of 4-chlorotoluene
b) %Conversion was determined by NMR and is the average of two runs

allowed for near complete reduction after only 2 hours. Upon factoring in the low cost and mildness of PMHS[1] and the desire to maximize reaction efficiency as well as ease of purification and workup, 4 equiv. PMHS and 2 equiv. of KF were settled on as the conditions of choice.

Having determined the optimal ratio and concentration of KF and PMHS, a screening of palladium salts was conducted against four chloroarenes to eliminate any false positive results. Two of the palladium salts, $Pd(CN)_2$ and $Pd(NH_2)Cl_2$, failed to reduce 4-chlorotoluene (Table 4, entries 1-2) and thus were not screened against the other chloroarenes. 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 $Pd(OAc)_2$ (per results in Table 6) 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. The use of palladium catalyst containing phosphine ligands, or the addition of phosphine ligands completely inhibited the reduction (entry 15). The source of palladium acetate also had a dramatic effect on reaction efficiency. Only 50% reduction occurred with 98% $Pd(OAc)_2$ purchased from Aldrich, where as complete conversion occurred with 99.5% $Pd(OAc)_2$ from Aldrich, and 98% $Pd(OAc)_2$ from Strem. All reactions were conducted with $Pd(OAc)_2$ bought from Strem.

Low molecular weight silanes and siloxanes fall short as compared to PMHS. PMHS is by far the least expensive, with the next cheapest silane being triethylsilane[48] costing ~$91 per mole of hydride, versus ~$7 per mole of hydride

Table 4. Screening of Palladium Sources for Chlorodehalogenation[a]



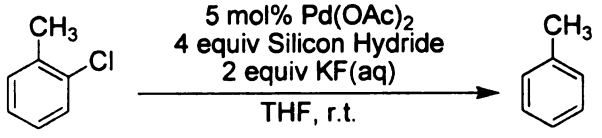
Entry	Catalyst	Substrate	Time (h)	Product	%Yield[b]
1	$Pd(CN)_2$	4-Chlorotoluene	3	Toluene	0
2	$Pd(NH_2)Cl_2$	4-Chlorotoluene	3	Toluene	0
3	$Pd(acac)_2$	4-Chlorotoluene	3	Toluene	73
4	Pd Black	4-Chlorotoluene	3	Toluene	94
5		4-Chloroaniline	0.5	Aniline	96
6		2-Chloropyridine	1.5	Pyridine	0
7	$PdCl_2$	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-Cloroaniline	0.5	Aniline	74
13		2-Chloropyridine	1.5	Pyridine	75
14		2-Chloro-*m*-xylene	17	Xylene	50
15	$Pd(OAc)_2 + PPh_3$	4-Chlorotoluene	24	Toluene	0

a) All reactions were performed on a 1 mmol scale
b) Determined by ^1H NMR with an internal standard (CH_2Cl_2), average of two runs.

for PMHS.[49] PMHS is air and moisture stable, can be measured directly from the bottle, and stored on the bench with no concerns. This is also the case for silanes, such as triethyl-, triphenyl-, triisopryl-, etc. Siloxanes containing hydrolysable functional groups, MeO, EtO, TMSO, on the other hand are air and moisture sensitive, requiring special measures when measuring out and storing[50] and are known hazardous compounds.[51] The use of PMHS for the chloroarene hydrodehalogenations would appear to be the optimal choice, but additional factors need to be taken into account. Since, PMHS is reacting with $Pd(OAc)_2$ to form palladium nanoparticles, which is the active catalyst for the dehalogenation, palladium nanoparticles with different particle sizes and/or surface textures could be formed from alternate siloxanes or silanes; in turn, influencing the efficiency and selectivity of the reduction. For that reason, a variety of silanes and siloxanes were tested in the dehalogenation of 2-chlorotoluene to toluene with

the $Pd(OAc)_2$/KF(aq)/THF combination (Table 5). Four of the silicon hydride reagents (entries 1,2, 6, and 9) efficiently promoted the reduction (>80%), with PMHS affording the highest yield of toluene, by ~10%.

Table 5. Screening of Silanes/Siloxanes in the Dehalogenation of 2-Chlorotoluene[a]



Entry	Silicon Hydride	% Yield[b]
1	PMHS	95
2	Et_3SiH	83
3	TMS_3SiH	50
4	$EtO(Me)_2SiH$	47
5	$TMSO(Me)_2SiH$	50
6	$Me(MeO)_2SiH$	84
7	$Me(TMSO)_2SiH$	50
8	$(TMSO)_3SiH$	32
9	1,3-Bis(trimethylsiloxy)-1,3-dimethyldisiloxane	87
10	methylhydrocyclosiloxanes	5

a) Performed on a 1 mmol scale
b) Determined by ^1H NMR with an internal standard (CH_2Cl_2), average of two runs.

3.3 Chloroarene Substrate Screening in the $Pd(OAc)_2$/PMHS/KF System

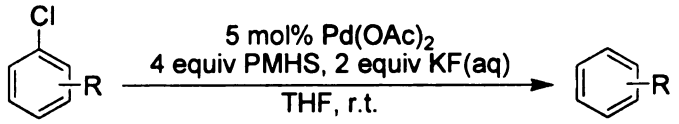
Having determined the optimal conditions[52] to be 5 mol% $Pd(OAc)_2$, 4 equiv. PMHS, 2 equiv. of an aqueous KF solution, and THF, a representative cross section of aromatic chlorides was tested (Table 6). Iodo-, bromo-, and chlorobenzene were efficiently reduced to benzene in 20 minutes (entry 1-3). 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 24-26) also perform well under the reaction conditions, even 2-chloropyridine, which has afforded poor yields in other

systems.[53] Dihalogenated arenes can also be reduced with 4 equiv. of PMHS per halogen[54] (entries 30, 33-35). These conditions are compatible with a variety of functional groups including ethers (entry 10), amines (entries 11-13), esters (entries16-17), amides (entries18-19), nitriles (entries 20-21), ketones (entry 27[55]), aryl fluorides (entry 22-23), and borate esters (entry 28[56]).

As was the case in the $Cl_2Pd(PPh_3)_2$ system, β-chlorostyrene was reduced to ethylbenzene (entry 36) in 3 hours at room temperature by the palladium nanoparticles. Unlike the original dehalogenation system, the $Pd(OAc)_2$/PMHS/KF combination effortlessly reduced styrene to ethylbenzene in 30 minutes, without a halide additive. The system was also capable of quantitatively reducing phenylacetylene to ethylbenzene.

A cross-section of functional groups influenced the dehalogenation, either causing the reduction to be sluggish, retarding the reaction all together, or changing the selectivity. For example, 4-(4-chlorophenyl)butan-2-one required an 18 hour reaction time for complete consumption of the chloride. Through the application of the palladium nanoparticles, formed from PMHS and $Pd(OAc)_2$, to the reduction of organic functional groups (also see Chapters 4 and 5), it became apparent that these nanoparticles are electrophilic; more specifically, they are oxophilic with a slight Lewis acidity. So, the extended reaction time for 4-(4-chlorophenyl)butan-2-one may be explained by the reversible coordination of the palladium nanoparticles to the aliphatic ketone. Of the substrates studied only 4-chlorophenol (entry 8) and 4-chlorobenzoic acid (entry 14) did not reduce. Unexpectedly though, subjection of 4-bromophenol and 4-bromobenzoic acid to

Table 6. Substrate Screening of the $Pd(OAc)_2$/PMHS/KF system



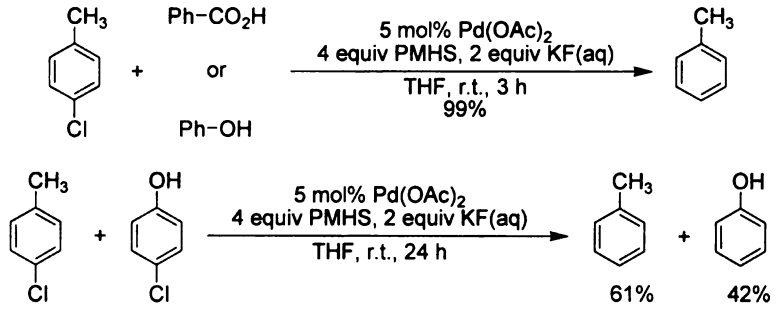
Entry	Starting Material	Time (h)	Product	%Yield[b]
1	Iodobenzene	0.33	Benzene	96
2	Bromobenzene	0.33	Benzene	96
3	Chlorobenzene	0.33	Benzene	95
4	4-Chlorotoluene	3	Toluene	95
5	2-Chlorotoluene	3	Toluene	100
6	2-Chloro-*m*-xylene	8	Xylene	100
7	1-Chloronaphthalene	4	Naphthalene	96, 82[c]
8	4-Chlorophenol	17	Phenol	0
9	4-Bromophenol	1	Phenol	99
10	4-Chloroanisole	1.5	Anisole	100
11	4-Chloroaniline	0.5	Aniline	99, 87[c]
12	3-Chloroaniline	0.75	Aniline	94
13	2-Chloroaniline	0.75	Aniline	99
14	4-Chlorobenzoic acid	24	Benzoic acid	0
15	4-Bromobenzoic acid	1	Benzoic acid	99
16	Methyl 4-chlorobenzoate	3	Methyl benzoate	84
17	Methyl 2-chlorobenzoate	1	Methyl benzoate	98, 76[c]
18	4-Chlorobenzamide	1.5	Benzamide	99, 83[c]
19	2-Chlorobenzamide	0.75	Benzamide	89
20	4-Chlorobenzonitrile	0.5	Benzonitrile	81
21	2-Chlorobenzonitrile	1	Benzonitrile	90
22	4-Chlorobenzotrifluoride	4	Benzotrifluoride	96
23	2-Chlorobenzotrifluoride	4	Benzotrifluoride	99
24	4-Chloropyridine•HCl	1.5	Pyridine	96
25	3-Chloropyridine	1	Pyridine	97
26	2-Chloropyridine	1.5	Pyridine	94
27	4-(4-Chlorophenyl)butan-2-one	18	4-Phenyl-butan-2-one	95, 85[c]
28	3-Chloro-5-methylphenylpinacolborane	6	3-Methylphenyl-pinacolborane	85[c]
29	1-Chloro4-fluorobenzene	20	Fluorobenzene	92
30	1-Bromo-4-chlorobenzene	24	Benzene	98
31	1-Chloro-4-iodobenzene	3	Chlorobenzene	93
32	1-Bromo-4-iodobenzene	3	Bromobenzene	90
33[d]	1,4-Dichlorobenzene	3	Benzene	98
34[d]	1,3-Dichlorobenzene	6	Benzene	98
35[d]	1,2-Dichlorobenzene	18	Benzene	98
36	β-Chlorostyrene (E/Z = 3/1)	3	Ethylbenzene	99

a) Performed on 1 mmol scale
b) Yields were determined by ^1H NMR with an internal standard (CH_2Cl_2), average of two runs
c) Isolated yields
d) Run with 4 equiv of PMHS and 2 equiv KF per halogen

the reaction conditions, quantitatively afforded the dehalogenated product in 1 hour. Intrigued by this result, control reactions were conducted to probe the inability of the catalyst system to reduce the aforementioned chlorinated

substrates. Reduction of 4-chlorotoluene in the presence of 1 equivalent phenol or benzoic acid afforded toluene in the same time and yield as originally observed. This signified that the phenol and carboxylic acid functional groups were not impeding the reduction. At this point 4-chlorotoluene was retested, but now in the presence of 1 equivalent 4-chlorophenol. This yielded toluene (61%) and phenol (42%) (Scheme7). The fact that 4-chlorophenol is unreactive, unless in the presence of 4-chlorotoluene, leads us to the conjecture that an aromatic palladium(II) chloride may be the active catalyst in the hydrodehalogenation. The opposite result was obtained when attempting to reduce 4-chlorobenzoic acid in the presence of 4-chlorotoluene. Here only partial formation of toluene occurred. Regrettably, the definitive reason why 4-chlorophenol and 4-chlorobenzoic acid are unreactive remains unknown at this time.

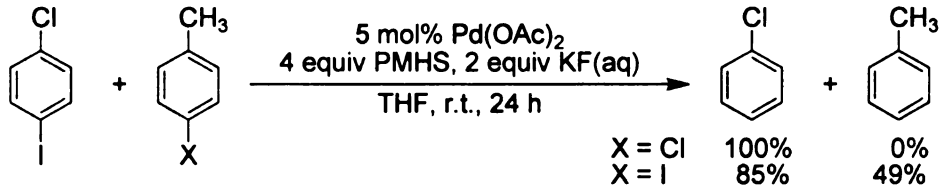
Scheme 7. Control Experiments to Determine OH and CO_2H Compatibility



A number of peculiar results were also encountered with the dihalogenated substrates. The reduction of 1-chloro-4-fluorobenzene (entry 29) was only 78% complete by GC after 12 hours and required 20 hours before the reaction was finished. Most unusual was the hydrodehalogenation of 1-chloro-4-iodobenzene (entry 31). Even though chlorobenzene and iodobenzene are

reduced in less than 30 minutes, after 3 hours only chlorobenzene was observed.[57] A similar result was encountered with 1-bromo-4-iodobenzene (entry 32) in which bromobenzene (96%) was the major product along with a small quantity of benzene (4%). Intrigued by the result that only iodine is reduced in entries 31 and 32, and both halogens are reduced in 1-bromo-4-chlorobenzene, control reactions were conducted to unveil the cause of this effect. Reaction of 1 equivalent of 1-chloro-4-iodobenzene in the presence of 1 equivalent of 4-chlorotoluene produced chlorobenzene with no observable reduction of the 4-chlorotoluene. Reducing 1 equivalent of 1-chloro-4-iodobenzene in the presence of 1 equivalent of 4-iodotoluene produced chlorobenzene and toluene (Scheme 8). The addition of more PMHS or $Pd(OAc)_2$ to the reaction after the initial reduction resulted in no further reduction of the chlorobenzene. Reduction of iodobenzene followed by the addition of 4-chlorotoluene afforded no toluene, where as the addition of 4-iodotoluene yielded toluene. This clearly demonstrated that the catalyst is not dead after the reduction of the iodoarene. A combination of 0.1 equivalent 4-iodotoluene and 4-chlorotoluene only results in reduction of the iodide. It was expected that reduction of an aromatic iodide would be more facile with the $Pd(OAc)_2$/PMHS/KF system, but as to why the system becomes completely selective for iodides is not understood. Taking into account the results with 4-chlorophenol, the formation of a palladium(II) specie as the active catalyst might explain the iodine selectivity. If a halide is a ligand on the active catalyst, then varying the halide from I, to Br, to Cl, could have a dramatic affect on the catalysts selectivity, and over all reactivity.

Scheme 8. Establishing the Selectivity of the Pd-Nanoparticles for Iodoarenes



3.4 Catalyst Loading

Having shown the reduction of chloroarenes by palladium nanoparticles with fluoride activated PMHS 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 7). Though longer reaction times were required, the hydrodehalogenations of 4-chlorotoluene, 4-chloroaniline, and methyl 2-chlorobenzoate were all high yielding in the presence of only 0.5 mol % $Pd(OAc)_2$ (entries 3, 7, and 11 respectively). Decreasing the catalyst loading further to 0.1 mol %, still allowed for the efficient, though slow, dechlorination of 4-chloroaniline and methyl 2-chlorobenzoate (entries 8 and 12). However, for 4-chlorotoluene (entry 4) diminishing returns set in at this loading.

Table 7. Adjustment of the Catalyst Loading in Chloroarene Dehalogenation[a]

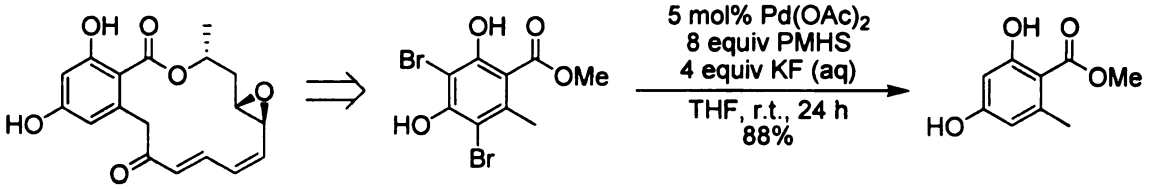
Entry	mol% $Pd(OAc)_2$	Substrate	Time (h)	Product	%Yield[b]
1	5	4-Chlorotoluene	3	Toluene	95
2	1	4-Chlorotoluene	10	Toluene	96
3	0.5	4-Chlorotoluene	24	Toluene	96
4	0.1	4-Chlorotoluene	54	Toluene	24
5	5	Methyl 2-chlorobenzoate	1	Methyl benzoate	98
6	1	Methyl 2-chlorobenzoate	9	Methyl benzoate	100
7	0.5	Methyl 2-chlorobenzoate	24	Methyl benzoate	99
8	0.1	Methyl 2-chlorobenzoate	54	Methyl benzoate	100
9	5	4-Chloroaniline	0.5	Aniline	99
10	1	4-Chloroaniline	1	Aniline	98
11	0.5	4-Chloroaniline	4	Aniline	98
12	0.1	4-Chloroaniline	29	Aniline	97

a) Conditions: 1 mmol chloroarene, $Pd(OAc)_2$, PMHS (4 mmol), KF (2 mmol), 5 mL THF, and 2 mL H_2O at room temperature.
b) Yields were determined by ^1H NMR with an internal standard (CH_2Cl_2), average of two runs

3.5 Applications of the $Pd(OAc)_2$/PMHS/KF System

After ascertaining the capabilities and limitations of the dehalogenation system, it was applied to a total synthesis and in conjunction with other methodology. As part of a total synthesis venture aimed at the construction of Monocillin I,[58] methyl 3,5-dibromo-2,4-dihydroxy-6-methylbenzoate was prepared. The next step called for reduction of both bromides. This was initially attempted under organotin radical conditions developed by our group. However the radical method failed to dehalogenate the dibromoarene, so a number of classical dehalogenation methods were examined. All gave unsatisfactory results. The desired product was obtained in high yield after subjection of the dibromoarene to the conditions laid out here: 5 mol% $Pd(OAc)_2$, 8 equivalents PMHS, 4 equivalents KF, in a THF/H_2O mixture (Scheme 9). The only apparent shortcoming in the reduction of the dibromoarene was the 24-hour reaction time.

Scheme 9. Application in the Total Synthesis of Monocillin I

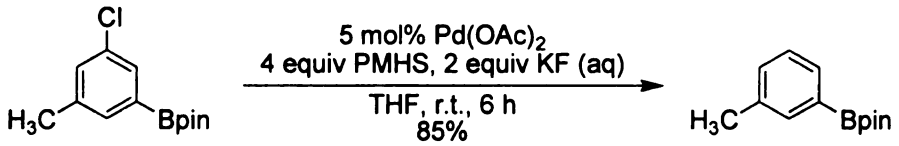


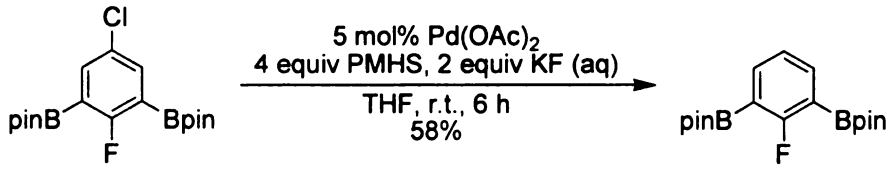
Monocillin I

We also looked to apply our chemistry in the service of other methodology. For example, Smith and co-workers have developed an iridium catalyst capable of performing C-H activation boralation on aromatics, with selectivity determined by sterics rather than electronics. Mono-substituted arenes typically afford a statistical mixture of *meta* and *para* pinacol boranes. To exclusively produce the *meta* isomer one could simply place a blocking group

meta to the monosubstituted position. This would force C-H activation borylation to the remaining *meta* position. Once borylation is complete the blocking group could be removed thereby affording the 3-substituted arylborane. A chloride is a good choice for the directing group. As previously stated, a large variety of aromatic chlorides are commercially available, inexpensive, and extremely stable. Moreover arylchlorides are excellent substrates in the catalytic borylations. Unfortunately initial attempts to reduce a chlorinated arylboronic ester resulted in concomitant degradation of the boronic ester. A collaboration with the Smith group was established to investigate if the palladium nanoparticles with fluoride activated PMHS could reduce a halogen directing group while not degrading or reacting with the boronic ester. The C-H activation, boralation, dehalogenation was originally attempted one-pot, unfortunately these efforts were unsuccessful, due to the added phosphine ligands for the iridium catalyst killing the palladium nanoparticles. When the aromatic pinacol borane was isolated and purified and then subjected to the dehalogenation conditions, the dehalogenated aromatic pinacol borane was afforded in moderate to high yields (Scheme 10).

Scheme 10. Dehalogenation Combined with a C-H Activation Borolyation





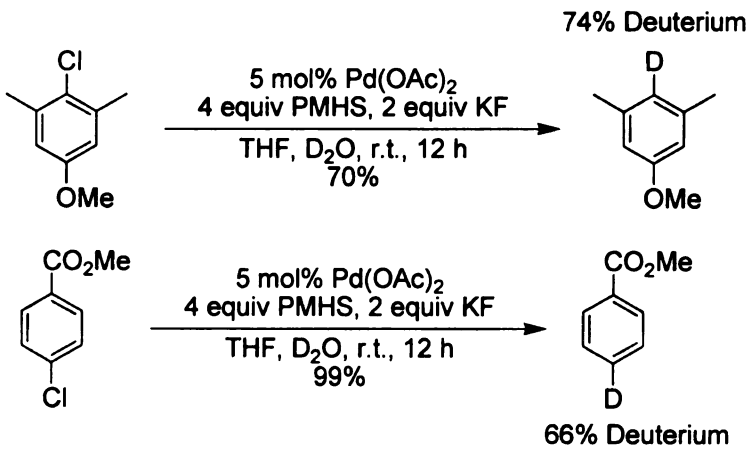
The groups of Deprés[59] and Gotor[60] have also found applications for the $Pd(OAc)_2$/PMHS/KF system, along with the kilo lab at Johnson and Johnson, and a medicinal chemist at Astellas.[61]

3.6 A Curious Water Effect

Serendipitously, it was found that the ratio of water to THF could influence the course of the reduction. Increasing the water/THF ratio from 2/5 to 3/5 decreased the required reaction time for the reduction of 4-chlorotoluene from three hours to one. However, the optimal amount of water for the reaction proved a delicate balance. Further increases in the amount of water prohibited the reaction from going to completion, while running the reduction under anhydrous conditions caused the reaction mixture to gel. The necessity of water, suggests that the reduction may take place via hydrogenation, with the hydrogen gas formed from a Si-H species and water with the aid of palladium.[62] To test the feasibility of a hydrogenation mechanism versus a transfer hydrogenation process (as proposed in Scheme 5), 2-chloro-5-methoxy-1,3-dimethylbenzene was used in two deuterium labeling experiments. In the first experiment, the aforementioned chloride was subjected to the reaction conditions with deuterated triethylsilane (Et_3Si-D). Unfortunately this yielded only starting material. Next, the aromatic chloride was resubjected to reaction conditions in the presence of deuterium oxide (D_2O). A 70% reduction of the chloride occurred, with 74% deuterium incorporation. To substantiate this result methyl 4-chlorobenzoate

was reduced in the presence of deuterium oxide, quantatitively affording methyl benzoate with 66% deuterium incorporation. If reduction of the halide took place by a hydrogenation process, the maximum deuterium incorporation should have been only 50%. Taking into account the results of 4-chlorophenol, 4-chlorobenzoic acid, and the iodine substrates, with the high level of deuterium incorporation from D_2O, a palladium(II)-palladium(IV) catalytic cycle may be the process of reduction, but at this point it is unknown as to how the chloroarenes are reduced. Vollhardt and Blum have also seen an effect from water with the $RhCl_3$-Aliquat 336 catalyst, where the rate of reduction is influenced by the water concentration, and the use of D_2O affords deuterium incorporation in the reduction of arenes[63] and arylacetylenes.[64] The role of the water in the mechanism of reduction with the rhodium catalyst is unknown.

Scheme 11. Deuterium Incorporation From D_2O

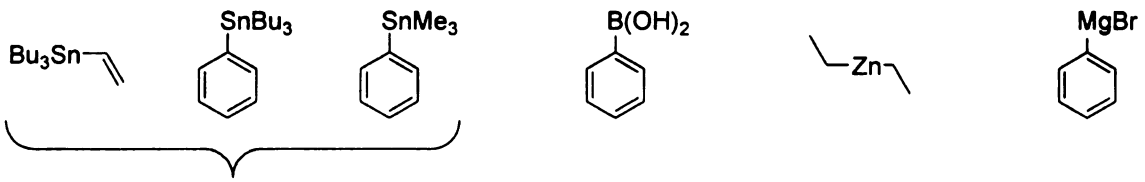


3.7 Attempted Extension of the Palladium Nanoparticles into Carbon-Carbon Cross-Couplings with Aromatic Chlorides.

The ability of the palladium-PMHS nanoparticles to readily reduce aromatic chlorides at room temperature, with broad functional group tolerance,

brought about the very exciting possibility of applying the palladium-PMHS nanoparticles to cross-coupling reactions with aromatic chlorides. The cross couplings were attempted with pre-formation, and in situ formation of the palladium nanoparticles from 5 mol% $Pd(OAc)_2$ and 20 mol% PMHS. A representative cross section of coupling partners was screened (Scheme 12) against a systematic variation of reaction conditions: solvent, temperature, and additives. The solvents screened ranged from aprotic non-polar to aprotic and protic polar (hexanes, toluene, CH_2Cl_2, $CHCl_3$, Et_2O, THF, 1,4-dioxane, DME, acetone, EtOAc, CH_3CN, NMP, DMF, MeOH, *i*-PrOH, H_2O), the reactions were run at room temperature, 50 °C, 70 °C, and 110 °C, in round bottoms and sealed tubes. The prototypical bases, and additives for each coupling partner were also screened. In every case tested, the cross coupled product could not be detected; only the electrophile and a small amount of the reduced electrophile were detected by GC or NMR. Even though oxidative addition of the aromatic chloride to the palladium nanoparticles occurs, it appears that the palladium is too electrophilic to allow transmetalation.

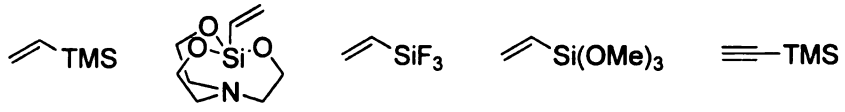
Scheme 12. Coupling Partners Screened



Based on the fact that the hydride of PMHS is transferred in the reduction process, led to the supposition that silicon reagents may be capable of transferring a carbon group. As previously, the Hiyama couplings were

conducted with pre-formation and in situ formation of the palladium nanoparticles. The coupling of 4-chlorotoluene with four vinyl silanes/siloxanes (Scheme 13) was conducted at room temperature and 70 °C, in round bottom flasks and sealed tubes, with a variety of silicon activators (KF, CsF, TBAF, Triton B, nBu$_4$NOH, H_2SiF_6, K_2SiF_6, $(NH_4)_2SiF_6$, KHF_2, and Me_3SiOK). All reactions were done in freshly distilled dry THF, and a THF/H_2O mixture. No other solvents were screened. After obtaining the same results as the previously attempted cross couplings, no detectable product, trimethylsilylacetylene was screened for it is more polarizable. Regretfully, cross coupling did not take place again.

Scheme 13. Hiyama Coupling Partners Screened



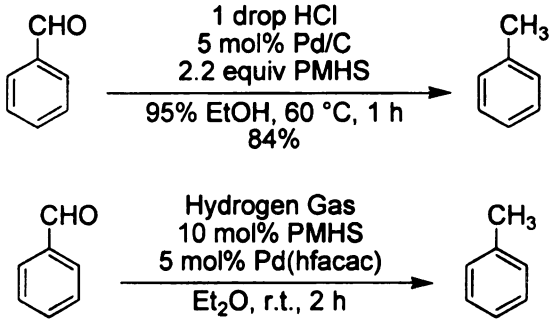
Chapter 4. Application of Palladium Nanoparticles in the Chemoselective Reduction of Benzylic Ketones, and the Chemo-, Regio-, and Stereoselective Reductive Cleavage of Benzylic C-O Bonds Promoted by an Aromatic Chloride

4.1 Introduction

Of the methods developed for deoxygenation of C-O bonds, Barton-McCombie,[65] Clemmensen,[66] and Wolff-Kishner[67] reactions are the most utilized methods in organic synthesis[68] and complement each other. Despite their wide use, these reactions can have unattractive features (harsh reaction conditions, low yields, limited functional group tolerance). As such, the creation of improved deoxygenation methods is still needed. This is exemplified by recent modifications of the Barton-McCombie and Wolff-Kishner reaction. Fu has modified the Baron-McCombie deoxygenation to be run with the in situ formation of tin hydride, from a catalytic amount of tin oxide, affording the products in higher yields and extending the reaction substrate set to include primary aliphatic alcohols.[69] Wood and co-workers developed a trialkylborane mediated variant that replaces the toxic tin hydride with water.[70] The use of 1,2-bis(*tert*-butydimethylsilyl)hydrazine in the formation of *N*-*tert*-butyldimethylsilylhydrazone derivatives allows the Wolff-Kishner reduction to be run under considerably milder reaction conditions and with increased efficiency.[71] The development of improved deoxygenation methods has only sparingly used silicon hydride reagents for this process. Triethylsilane-TFA[72] promotes the deoxygenation of tertiary alcohols,[73] and benzylic carbonyls.[74] The combination of a silicon hydride

and the Lewis acid $B(C_6F_5)_3$ catalyzes the deoxygenation of benzylic carbonyls, benzylic alcohols, and primary alcohols.[75] In two cases, PMHS has been used with a palladium catalyst to reduce benzaldehyde to toluene (Scheme 14).[76,45] Notwithstanding the use of silicon hydrides in deoxygenation procedures, there still lies room for improvement, and the limited exploration of palladium catalysts with silicon hydrides to promote this reduction, warrants further investigation.

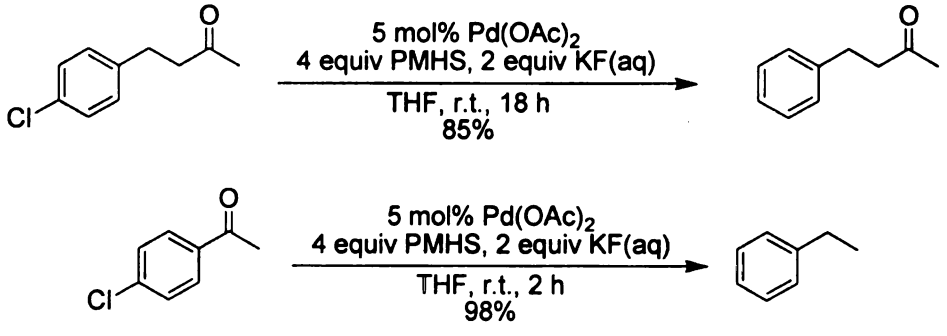
Scheme 14. Applications of PMHS in the Deoxygenation of Benzaldehyde[45,76]



Based on a theory, that fluoride activated PMHS could form organotin hydrides from organotin halides, led to the development and application of in situ prepared trialkyl tin hydrides from PMHS.[5,6] This method ultimately resulted in a one-pot hydrostannation / Stille coupling catalytic in tin. In the developing stage of this tandem reaction it was though that fluoride activated PMHS in combination with a palladium catalyst may reduce the halogen electrophile. This proved not to be an issue, but the question then arose, can fluoride activated PMHS and a palladium catalyst promote a hydrodehalogenation? In answering this question, a homogenous palladium catalyzed dehalogenation method was found, using $Cl_2Pd(PPh_3)_2$, PMHS, and aqueous KF (Chapter 2).[16a] Aromatic iodides, bromides, and α-keto bromides are reduced with this method, but aromatic chlorides are unaffected. A desire to modify the system to include aromatic

chlorides, led to the finding that PMHS reacts with $Pd(OAc)_2$ to form palladium nanoparticles, which in combination with PMHS and aqueous KF will rapidly hydrodehalogenate aryl chlorides at room temperature (Chapter 3). While screening substrates in the $Pd(OAc)_2$/PMHS/KF dehalogenation system, it was found that only the halide of 4-(4-chlorophenyl)-2-butanone (Scheme 15) was reduced, whereas in the case of 4'-chloroacetophenone (Scheme 15), 2-chloroacetophenone, and 4-chlorobenzaldehyde the reaction conditions also promoted deoxygenation of the carbonyl. We were intrigued by the apparent chemoselectivity, efficiency, and mildness of these deoxygenations. The literature[77] suggested that further development of this method could be synthetically useful and more importantly that this deoxygenation might be mechanistically unique.

Scheme 15. Over Reduction of 4'-Chloroacetophenone to Ethylbenzene

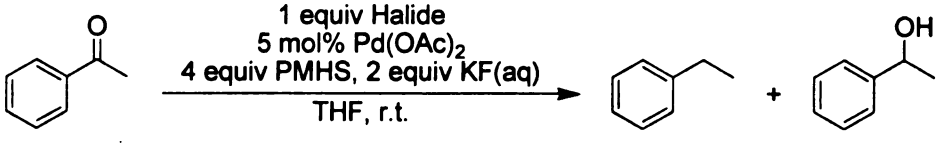


4.2 Optimization of the Deoxygenation Conditions

To explore the generality of the deoxygenation, acetophenone was subjected to the dehalogenation conditions. Surprisingly, only reduction of the carbonyl to the alcohol was observed (Table 8, entry 1). The missing component from the initial deoxygenation test was the presence of the chloride. An investigation was initiated to find if this chloroarene was affecting the reaction

due to its intramolecular communication with the benzylic carbonyl group, or if an external halide source could promote the deoxygenation (Table 8). It was found that chlorobenzene (entry 2) efficiently facilitates deoxygenation, where as bromo- and iodobenzene (entries 3 & 4) are inefficient and ineffective in promoting reduction of the carbonyl to the methylene. To examine if the chloride source needed to be aromatic a number of chloride salts were tested (entries 5-7), all of which resulted in only trace amounts of ethylbenzene being formed. From these results it was reasoned that chlorobenzene was facilitating deoxygenation through 1) the formation of an aromatic palladium(II) chloride, which is the active catalyst, 2) by the aromatic chloride ultimately serving as a source of HCl,[78] or 3) an admixture of these pathways. Having established that LiCl (entry 7) and phenyl nonaflate (entry 8) were unsuitable additives for deoxygenation on there own, the two were combined resulting in quantitative

Table 8. Screening of Halide Sources for Deoxygenation



Entry	Halide Source	Time (h)	%Yield[a]	%Yield[a]
1	None	24	0	98
2	Chlorobenzene	1	100	0
3	Bromobenzene	2	22	78
4	Iodobenzene	16	0	25
5	Bu_4NCl	3.5	Trace[b]	30
6	CsCl	24	Trace[b]	98
7	LiCl	24	Trace[b]	99
8	PhONf	1	Trace[b]	99
9	PhONf + LiCl	1	97	0
10	BnCl	1	100	0
11	1-Chlorobutane	1	Trace[b]	22
12	HCl	1	15	40

a) Determined by ^1H NMR with an internal standard (CH_2Cl_2), average of two runs
b) Determined by GC

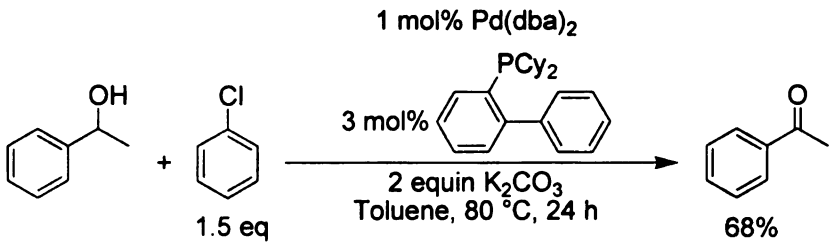
formation of ethylbenzene (entry 9) and confirming the formation of an aromatic palladium(II) chloride.[79,80] At this point HCl (entry 12) was examined affording only 15% ethylbenzene, but it should be noted that *sec*-phenethyl alcohol was completely deoxygenated when in the presence of HCl. Benzyl chloride (entry 10) was also found to be a suitable additive, where as 1-chlorobutane (entry 11) was not effective.

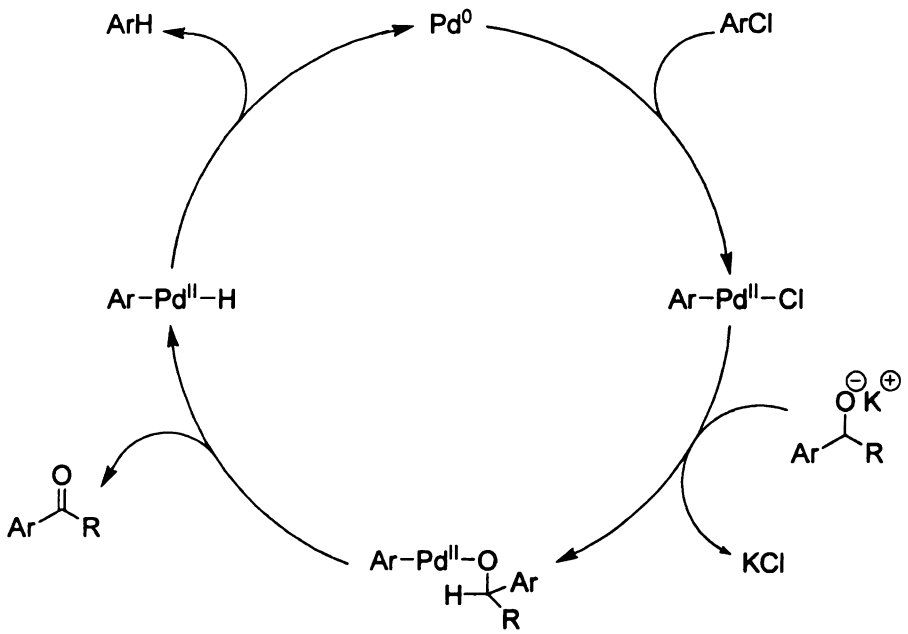
It was reasoned that if an aromatic (or benzylic) palladium(II) chloride species was catalyzing the reduction, then only a catalytic amount of chlorobenzene should be needed to form the active catalyst. The chlorobenzene concentration was systematically lowered showing that as low as 1 mol% chlorobenzene could be used with 5 mol% $Pd(OAc)_2$ to perform the deoxygenation, but lowering the concentration below 1 mol% only resulted in reduction to the alcohol. The productive utilization of chlorobenzene in palladium catalysis is known for the oxidation of benzylic alcohols to carbonyls, but stoichiometric levels are required (Scheme 16).[81] However, to the best of our knowledge this is the first example of PhCl being a productive additive in Pd-mediated reductions.

Optimization of the $Pd(OAc)_2$, PMHS, and KF concentrations were carried out on acetophenone with 0.1 equivalents of chlorobenzene (Table 9). It was determined that an increased KF concentration is required for lower catalyst loading and PMHS concentrations. Factoring in the cost of $Pd(OAc)_2$ and a desire to minimize the concentration of PMHS for easy of purification, 5 mol% $Pd(OAc)_2$, 2.5 equivalents PMHS, and 4 equivalents KF were settled on as the

conditions of choice (entry 4). As little as 1 mol% $Pd(OAc)_2$ can be used, but requiring 5 equivalents of PMHS and 10 equivalents of KF.

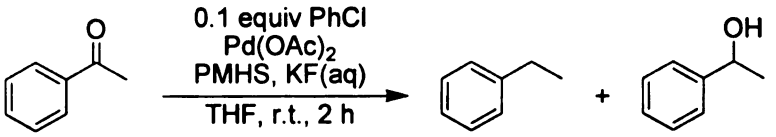
Scheme 16. Palladium Catalyzed Oxidation with Chlorobenzene





As stated in Chapter 3, a variety of silanes and siloxanes were screened in the deoxygenation, since the nanoparticles formed from alternate silicon hydride sources could have different sizes and surface textures, which would thereby influence the efficiency and reactivity of the catalyst. Only one of the siloxanes tested worked as well as PMHS (Table 10, entry 9).

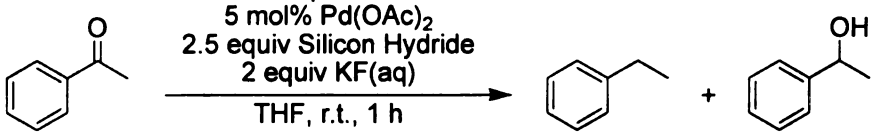
Table 9. Optimization of the $Pd(OAc)_2$, PMHS, and KF Concentrations



Entry	mol% $Pd(OAc)_2$	equiv PMHS	equiv KF	%Yield[a]	%Yield[a]
1	5	4	2	99	0
2	5	3	2	100	0
3	5	2.5	2	89	11
4	5	2.5	4	98	0
5	5	2	2	57	43
6	5	2	4	74	23
7	5	2	6	91	8
8	3	4	2	70	27
9	3	4	4	97	0
10	3	2	4	68	29
11[b]	1	4	2	0	70
12	1	4	4	45	53
13	1	4	6	93	6
14	1	4	8	98	0
15	1	2	8	52	45

a) Determined by ^1H NMR with an internal standard (CH_2Cl_2), average of two runs
b) 30% acetophenone

Table 10. Screening of Non-polymeric Silanes and Siloxanes for Deoxygenation



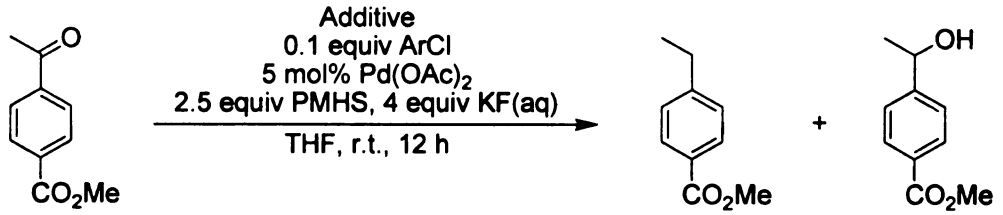
Entry	Silicon Hydride	%Yield	%Yield	% S.M.
1	PMHS	98	0	0
2	Et_3SiH	66	33	0
3	TMS_3SiH	46	53	0
4	$EtO(Me)_2SiH$	70	30	0
5	$TMSO(Me)_2SiH$	86	14	0
6	$Me(MeO)_2SiH$	0	14	82
7	$Me(TMSO)_2SiH$	89	10	0
8	$(TMSO)_3SiH$	0	0	100
9	1,3-bis(trimethylsiloxy)-1,3-dimethyldisiloxane	97	0	0
10	methylhydrocyclosiloxanes	20	70	5

a) Determined by ^1H NMR with an internal standard (CH_2Cl_2), average of two runs

4.3 Determining the Role of the Aromatic Chloride and Elucidating the Proposed Catalytic Cycle.

To determine the role of the aromatic chloride additive a variety of chloroarenes were screened, varying the sterics and electronics of the arene. To accurately establish the effects of the chloroarene, and easily identify increases and decreases in reduction efficiency, screening was conducted against methyl 4-acetylbenzoate, a substrate were only partial deoxygenation occurred with chlorobenzene. As seen in Table 11, the yield of deoxygenation was affected by the chloroarene used. The sterics of the xylene inhibited the reduction slightly (entry 2), where as 2-chloropyridine afforded only a small amount of the alcohol (entry 5). Four of the aromatic chlorides increased the yield of the methylene product (entries 3-4 and 6-7), as compared to chlorobenzene (entry 1), with 4-

Table 11. Determining the Role of the Aromatic Chloride



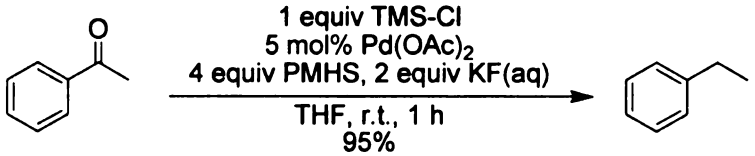
Entry	ArCl	Additive	%Yield[a]	%Yield[a]
1	chlorobenzene		21	77
2	2-chloro-*m*-xylene		13	74
3	4-chloroanisole		39	46
4[b]	4-chlorobenzotrifluoride		32	28
5[c]	2-chloropyridine		0	13
6	*o*-cichlorobenzene		38	61
7	hexachlorobenzene		30	66
8	4-chloroanisole	2,6-lutidine[d]	0	94
9	4-chloroanisole	DTBMP[e]	33	65
10	4-chloroanisole	Proton-Sponge®[e]	0	98
11	4-chloroanisole	propylene oxide[e]	37	57

a) Isolated yields after FC, average of two runs b) 10% starting material c) 85% starting material d) Run with 0.1 equivalents e) Run with 0.5 equivalents
DTBMP = 2,6-di-*tert*-butyl-4-methylpyridine

chloroanisole (entry 3) affording the highest yield. At this point, methyl 4-acetylbenzoate was subjected to the reaction conditions with 4-chloroanisole in the presence of an acid scavenger (entries 8-11). The addition of 2,6-lutidine or Proton-Sponge® suppressed the deoxygenation. These results suggested the slow release of HCl as the true additive promoting the deoxygenation. The increased yield upon changing the aromatic chloride could be attributed to slower rates of oxidative addition or reductive elimination, depending on the aromatic chloride in question.

To evaluate the HCl pathway, chlorotrimethylsilane (TMSCl) was used as an additive for the reduction of acetophenone (Scheme 12). Under the conditions found in Table 8 the reaction with this additive afforded ethylbenzene in 95% yield. The use of catalytic TMSCl (0.1 equiv) was also found to be effective with the substrates found in Table 13 entry 1 (94%) and entry 41 (25%). Subjection of the enatomericly pure epoxide (Table 14, entry 21) to the reaction conditions with 0.1 equiv TMSCl afforded the 1,2-diol in 97% and 90% de, similar to the result obtained with chlorobenzene.

Scheme 17. Evaluating the HCl Pathway with TMSCl

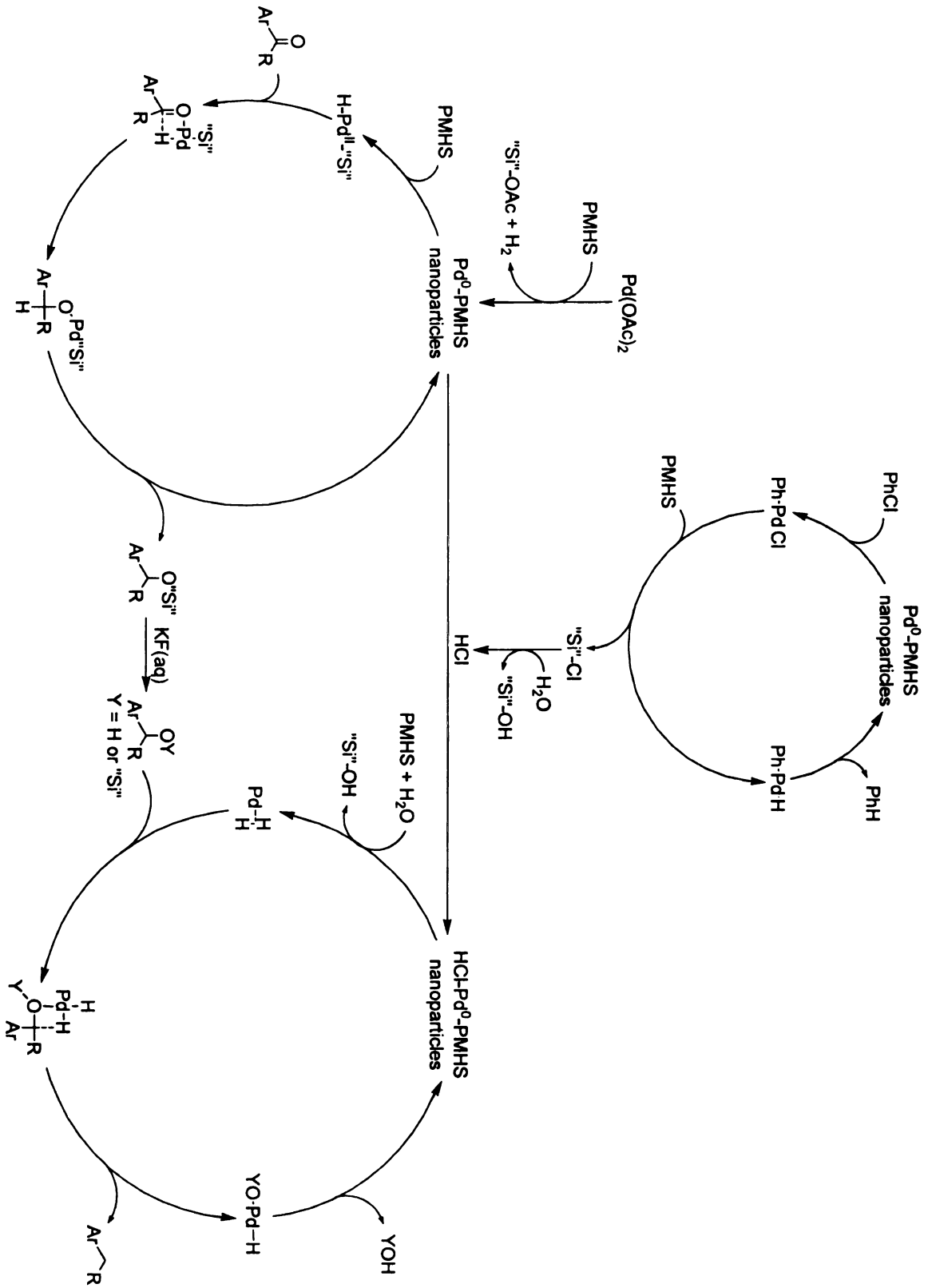


A number of simple control reactions were conducted to further elucidate a possible mechanism. Kobayashi[82] and Corriu[83] have demonstrated that PMHS and a fluoride source can reduce carbonyls to alcohols, so acetophenone was reacted with PMHS and aqueous KF in THF. This resulted in no reaction. As

stated earlier, subjection of acetophenone to the dehalogenation conditions only afforded the alcohol. So in the deoxygenation process, a palladium mediated reduction to the alcohol appears to occur first. Reduction of the carbonyl to the alcohol may be occurring through one of two pathways, palladium catalyzed hydrosilylation or hydrogenolysis. Deoxygenation of the alcohol only takes place when in presence of HCl, or an HCl surrogate: aromatic chloride, or TMSCl. From these results a two-step mechanism can be proposed (Scheme 13). The ketone is reduced to the alcohol by palladium catalyzed hydrosilation. In the interim, chlorobenzene is reduced to benzene and a chlorosiloxane, which is then hydrolyzed to HCl. The HCl is then absorbed onto the surface of the palladium nanoparticles, forming a new catalyst that deoxygenates the alcohol through hydrogenolysis, with the hydrogen gas being formed from the siloxane and water.[62]

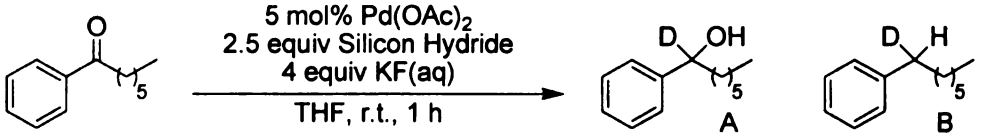
To lay creed to the two-step mechanistic pathway deuterium labeling experiments were conducted on 1-phenyl-octan-1-one (Table 12). Running the reduction in the absence of chlorobenzene, but with Et_3Si-D afforded the alcohol in 97% yield and 90% deuterium incorporation at the benzylic carbon, where as using PMHS with deuterium oxide quantitatively produced the alcohol with 3% deuterium incorporation (entries 1-2). These results clear showed that reduction of the carbonyl takes place by palladium catalyzed hydrosilation. From here, 1-phenyl-octan-1-one was subjected to the reaction conditions with chlorobenzene, where the use of Et_3Si-D yielded the methylene in 38% with 57.5% deuterium incorporation, and a yield of 92% with 36.5% deuterium incorporation taking

Scheme 18. Proposed Deoxygenation Catalytic Cycle



place with PMHS and D_2O (entries 3-4). Theoretically, 75% deuterium incorporation should occur when using Et_3Si-D, and 25% when using D_2O. Even though the numbers are too high in one case (D_2O), and to low in the other (Et_3SiD), the results substantiate the proposed mechanism as the major pathway, but not the only pathway. The deuterium results also showed that a small amount of the carbonyl reduction was occurring by hydrogenolysis, and the role of the aromatic chloride may be more than simple formation of HCl.

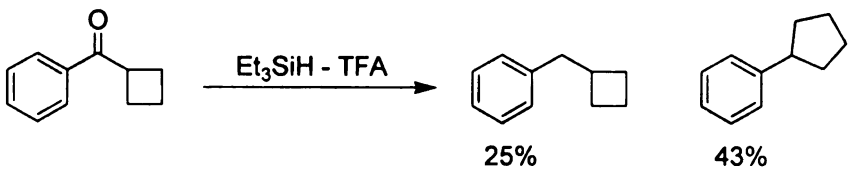
Table 12. Deuterium Labeling Experiments



Entry	PhCl	Silicon Hydride	Water	%Yield	%Deuterium Incorporation	Product
1	None	Et_3Si-D	H_2O	97	90	A
2	None	PMHS	D_2O	100	3	A
3	0.1 equiv	Et_3Si-D	H_2O	38	58.5	B
4	0.1 equiv	PMHS	D_2O	92	36.5	B

Cationic and radical pathways could be discounted based on the results of cyclobutyl phenyl ketone (Table 13, entries 7-11) and 1-(benzyloxy)-4-methoxybenzene. If the deoxygenation occurred through a radical or cationic mechanism, then cyclobutyl phenyl ketone would undergo ring expansion and ring opening,[84] which was not seen; and 1-(benzyloxy)-4-methoxybenzene would afford benzoquinone,[85] instead of producing 4-methoxyphenol (98%).

Scheme 19. Deoxygenation of Cyclobutyl Phenyl Ketone via Cationic Process.

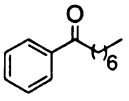
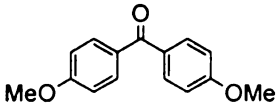
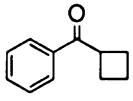
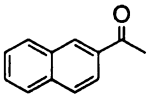
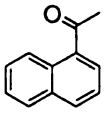
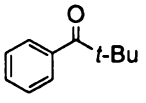
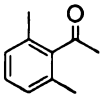
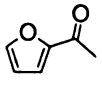
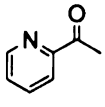
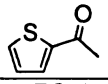


4.4 Deoxygenation Substrate Screening

Having explored the mechanism of the deoxygenation an investigation was next initiated to determine the selectivity of the reduction. The results of the initial substrate screening can be seen in Table 13 and 14, where the optimized reaction conditions, 5 mol% $Pd(OAc)_2$, 2.5 equivalents PMHS, 4 equivalents of aqueous KF, and 0.1 equivalents of chlorobenzene[86] were used. Increasing the steric hindrance alpha to the carbonyl decreased the efficiency of the deoxygenation (Table 13, entries 1-21). A secondary carbon alpha to the benzylic ketone was only partially deoxygenated (entry 7), however a benzophenone analog was easily reduced (entry 6). Simply changing the aromatic chloride to 4-chloroanisole promoted complete conversion to the methylene for phenyl cyclobutyl ketone (entry 10) and 1-acetylnaphthalen (entry 14). The sterics of a *t*-Bu group completely inhibited deoxygenation (entries 15-19), and 2-acetyl-*m*-xylene was unreactive all together (entries 20-21). In the absence of an aromatic chloride, the ketone was efficiently reduced to the alcohol regardless of the sterics alpha to the carbonyl (entries 5, 11, 19). The method was also successfully applied to 2-furyl methyl ketone (entry 22), but in the case of 2-acetylpyridine reduction to the alcohol only occurred (entry 24), this was attributed to the pyridine sequestering the in situ formed HCl. A small amount of alcohol could only be obtained from 2-acetylthiophene (entry 26), for the sulfur likely coordinates to the electrophilic palladium and kills the catalyst.

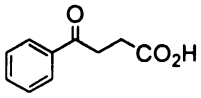
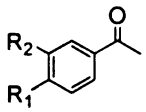
In terms of functional group tolerance, deoxygenation in the presence of a para phenol occured without incident (entries 30-31), whereas a meta phenol

Table 13. Initial Deoxygenation Substrate Screening

Entry	Starting Material	equiv PMHS	equiv KF	Chloride Source	%Yield Alcohol	%Yield Methylene
1[b]		5	10	PhCl	0	97
2[c]		4	4	PhCl	0	96
3		2.5	4	PhCl	0	92
4		2.5	4	TMSCl	0	95
5		1.5	2	None	88	0
6		2.5	4	PhCl	0	95
7		2.5	4	PhCl	21	72
8		4	4	PhCl	12	83
9[d]		4	4	PhCl	8	86
10		4	4	Chloroanisole	0	94
11		1.5	2	None	99	0
12		2.5	4	PhCl	0	84
13		2.5	4	PhCl	20	80
14		2.5	4	Chloroanisole	0	99
15[b]		5	10	PhCl	96	0
16		2.5	4	PhCl	96	0
17		4	4	PhCl	97	0
18[d]		4	4	Chloroanisole	96	0
19		1.5	2	None	99	0
20[e]		4	4	PhCl	0	0
21[e]		4	4	None	0	0
22[f]		2.5	4	PhCl	0	100
23[f]		2.5	4	PhCl	98	0
24[f]		2.5	4	PhCl	23	0

a) isolated yields after FC b) Run with 1 mol% $Pd(OAc)_2$ and stirred for 2 h c) Run with 3 mol% $Pd(OAc)_2$ and stirred for 2 h d) 0.5 equiv of chlorobenzene were used e) stirred for 24 h f) Yield determined by ^1H NMR with an internal standard (CH_2Cl_2)

Table 13. Initial Deoxygenation Substrate Screening, Continued

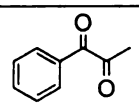
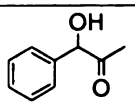
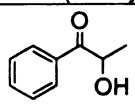
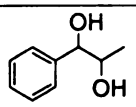
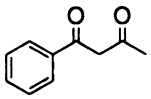
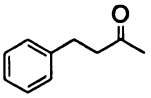
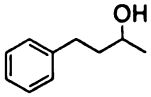
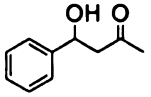
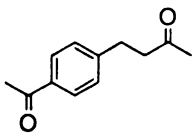
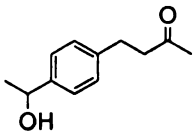
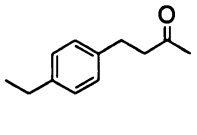
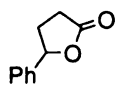
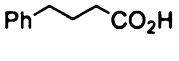
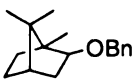
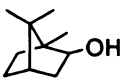
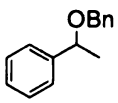
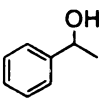
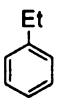
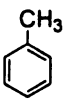
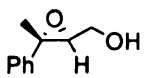
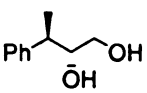
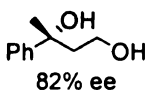
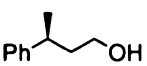
Entry	Starting Material	equiv PMHS	equiv KF	Chloride Source	%Yield Alcohol	%Yield Methylene
28		2.5	4	PhCl	91	9
29		1.5	2	None	92	0
						
30[b]	R_1 = OH	5	10	PhCl	0	94
31		2.5	4	PhCl	0	86
32[g]		1.5	2	None	67	0
33	R_2 = OH	2.5	4	PhCl	50	34
34[b]	R_1 = OMe	5	10	PhCl	0	95
35		2.5	4	PhCl	0	94
36[b]	R_1 = OAc	5	10	PhCl	93	5
37[h]	R_1 = NH_2	2.5	4	PhCl	69	16
38[i]	R_2 = NH_2	2.5	4	PhCl	36	0
39	R_1 = CO_2Me	2.5	4	PhCl	77	21
40		4	4	PhCl	73	25
41		4	4	TMSCl	71	25
42		2.5	4	Chloroanisole	57	39
43		4	4	Chloroanisole	46	52
44	R_1 = Ph	2.5	4	PhCl	25	72

b) Run with 1 mol% $Pd(OAc)_2$ and stirred for 2 h g) 40% starting material isolated h) 15% starting material isolated I) 59% starting material isolated

afforded the methylene in only 34% (entry 33). Aniline derivatives inhibited the reduction (entries 37-38), again likely due to sequestering of the in situ formed HCl. The carboxylic acid of 3-benzyoylproprionic acid caused catalyst inhibition, affording 4-phenylbutanoic acid in a low 9% yield, yet running the reaction in the absence of an aromatic chloride produced the alcohol in high yield (entries 28-29). Methyl 4-acetyl benzoate also saw partial reduction due to the catalyst coordinating to the carbonyl of the ester. Increasing the PMHS concentration had little effect in increasing the yields of the reduced products, but again simply changing the aromatic chloride to 4-chloroanisole increased the yield of methyl 4-ethylbenzaote by 27% (entries 40-41).

To evaluate the chemoselectivity of the system three dicarbonyl substrates were tested. Under the standard conditions deoxygenation did not occur for a 1,2-dicarbonyl, but 48% reduction of the benzylic ketone transpired along with formation of the 1,2-diol in 49%. The 1,2-diol produced was a mixture of anti and syn isomers, favoring the anti isomer (~3/1), with the assignment based on correlation of the ^{1}H NMR to an alternate synthesis of the same compound.[87] Hydrogenolysisof 1-phenylpropane-1,2-dione with PtO_2 afforded the syn 1,2-diol. Increasing the PMHS concentration to 5 equivalents produced the fully saturated product in 17%, as the only observed deoxygenated product. Poor selectivity was also seen when running the reduction in the absence of an aromatic chloride (Table 14, entries 1-4). Deoxygenation of the benzylic ketone took place with a 1,3-dicarbonyl in 79% when using 5 equivalents of PMHS, in combination with 46% reduction of the aliphatic ketone. Elimination of chlorobenzene from the reaction gave the benzylic alcohol in low yield (entries 5-9). Chelation of the palladium catalyst between the oxygen's of the 1,2- and 1,3-dicarbonyl likely produced the low selectivity. For that reason, 4-(4-acetyl-phenyl)-butan-2-one was prepared and subjected to the reaction conditions, which resulted in reduction of only the benzylic ketone (entries 10-14). As had been seen with prior substrates, putative coordination of the catalyst to the aliphatic carbonyl inhibited the reduction. Increasing the PMHS concentration had little effect on the efficiency, but the use of 4-chloroanisole increased the yield of the methylene product (entry 12).

Table 14. Evaluation of the Deoxygenation Selectivity

Entry	Starting Material	equiv PMHS	equiv KF	ArCl	Product(s) %Yield (anti/syn)		
							
1		2.5	4	PhCl	48	0	49 (2.6/1)
2[b]		5	4	PhCl	23	11	43 (3.0/1)
3		1.5	2	None	49	24	19 (1.5/1)
4		4	4	None	44	14	32 (1.7/1)
							
5[c]		5	10	PhCl	27	25	24
6		2.5	4	PhCl	7	11	48
7		5	4	PhCl	33	46	0
8		1.5	2	None	0	0	42
9		4	4	None	0	0	35
							
10		2.5	4	PhCl	44		52
11		4	4	PhCl	41		57
12		4	4	Chloroanisole	25		72
13[d]		1.5	2	None	47		0
14[e]		3	4	None	94		0
							
15		1.5	2	PhCl	90		
							
16[f]		2.5	4	PhCl	67		
17[g]		1.5	2	None	65		
							
18[h]		2.5	4	PhCl	3	94	96
19[h]		1.5	2	None	98	Trace	99
	 89.5% ee						
20		2.5	4	PhCl	97 (95% de)		
21		2.5	4	TMSCl	95 (90% de)		
22		1.5	2	None	99 (79% de)		
	 82% ee						
23		2.5	4	PhCl	62 (81% ee)		

Conditions: 1 mmol substrate, 5 mol% $Pd(OAc)_2$, PMHS, KF, 0.1 equiv ArCl, 5 mL THF, 2 mL H_2O, 1 hour
a) Isolated yields after FC b) 17% Propylbenzene by GC c) 1 mol% $Pd(OAc)_2$ used d) 53% starting material isolated e) 4% starting material isolated f) 31% starting material isolated g) stirred for 8 h h) Yield determined by ^1H NMR with an internal standard (CH_2Cl_2)

The system is not limited to benzylic carbonyls and alcohols, subjection of the TMS, DMPS, and Ac *sec*-phenethyl protected alcohol to the reaction conditions quantitatively yielded ethylbenzene. A lactone (entry 15) was selectively opened to the aliphatic carboxylic acid with the use of 1.5 equivalents of PMHS,[88] with and without chlorobenzene (entry 15). The reduction run with chlorobenzene was complete in 30 minutes, where the reaction run in the absence of chlorobenzene took 10 hours to go to completion. The high reactivity of the catalyst formed form chlorobenzene could also be seen with the benzyl-bornyl ether (entry 16-17) where the reaction was complete in less than one hour. Without PhCl only 15% of isobornyl alcohol was formed in one hour, and it took over 8 hours for the reaction to give a comparable yield. Another interesting discovery was the subjection of the di-benzyl ether (entry 18-19) to the reaction conditions, with PhCl, resulted in complete regioselective hydride delivery to the least substituted benzyl, affording toluene and *sec*-phenethyl alcohol in near quantitative yield.[89] To further evaluate the regioselectivity, and establish the stereoselectivity of the reduction, a benzylic epoxide (entry 20) with set stereochemistry was subjected to the conditions. This afforded the 1,2-diol in high yield and 95% de. Subjection of the epoxide to the conditions without chlorobenzene afforded the 1,2-diol quantitatively, but with a greatly decreased de (79%). Assuming the chloride is a ligand on the more reactive catalyst, rotation of the epoxide coordinated to the palladium may be restricted, and/or one face of the epoxide may be shielded. So, reduction of the epoxide in the absence of a chloride source leaves an open coordination site on the palladium,

allowing greater rotational freedom of the substrate and/or hydride delivery to occur from either face. The stereoselectivity of the system was further tested on a tertiary benzylic alcohol (entry 23) with a set stereocenter, affording (S)-3-phenyl-1-butanol with no loss of enantiomeric excess and retention of configuration, which at this point it is unknown as to how the catalyst deoxygenates the tertiary alcohol with retention of configuration.

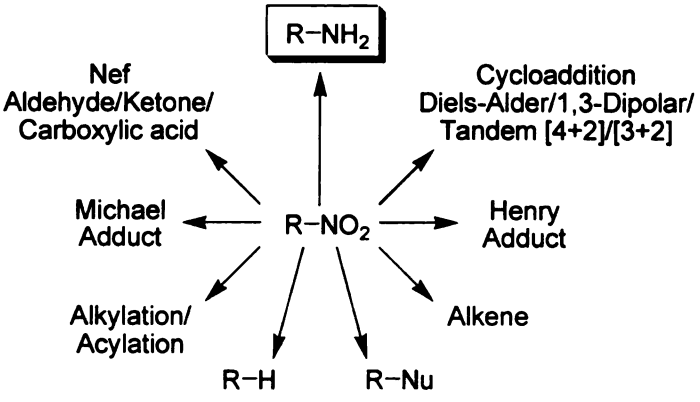
In summary, it was found that the addition on an aromatic chloride to the $Pd(OAc)_2$/PMHS/KF system promotes the reductive cleavage of benzylic C-O bonds. Investigation into the mechanism suggests the role of the aromatic chloride is slow controlled release of HCl, but the choice of aromatic chloride can have a pronounced affect on the reaction efficiency. The mechanism of deoxygenation is proposed to occur through palladium catalyzed hydrosilylation, followed by hydrogenolysis of the alcohol. Increasing steric hindrance alpha to the carbonyl decreases reaction efficiency, and basic functional groups capable of sequestering HCl impede the deoxygenation. The system can selectively reduce a benzylic ketone in the presence of an aliphatic ketone, deoxygenate a tertiary alcohol with retention of configuration, and reductively cleave a benzylic C-O bond of an epoxide, ether, and lactone.

Chapter 5. Palladium Catalyzed Reduction of Aromatic and Aliphatic Nitro Groups Promoted by a Silicon Hydride, and a One-Pot Reductive Conversion to Amides, Sulfonamides, and Carbamates

5.1 Introduction

A versatile class of building blocks in organic synthesis are nitro compounds (Scheme 20), which can be used in Henry and Michael reactions, the nitro group can be alkylated, acylated, halogenated, under go a Nef reaction, be substituted with a nucleophile or eliminated, participate in cycloaddition chemistry, and serve as a precursor to amines.[90] A vast number of nitroaromatics are commercially available or easily prepared.[90,91] and advances in asymmetric catalysis have made access to stereodefined aliphatic nitro compounds a viable route.[92,93,94] A plethora of methods have been developed for the reduction of nitro compounds to amines,[95] ranging from hydrogenation, transferhydrogenation, electron transfer, electrochemical, and hydride reductions. Despite the fact that several of theses methods are widely used, there still exists a need for new protocols[96] that are run under milder reaction conditions, are environmentally

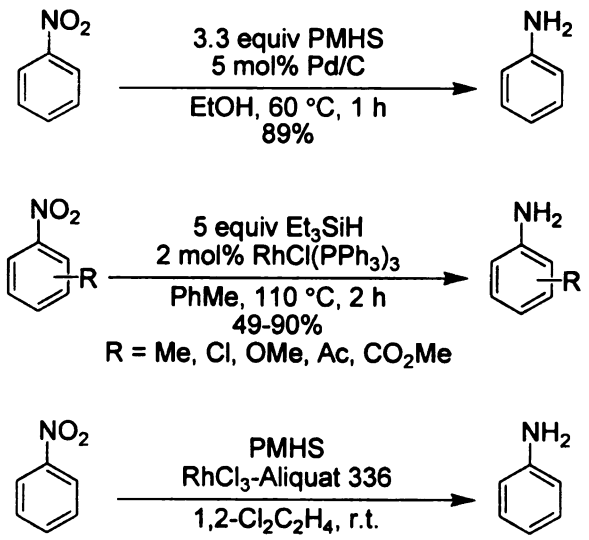
Scheme 20. Nitro Compounds: Versatile Building Blocks in Synthesis



friendly, amendable to combinatorial synthesis, and/or have high functional group compatibility.

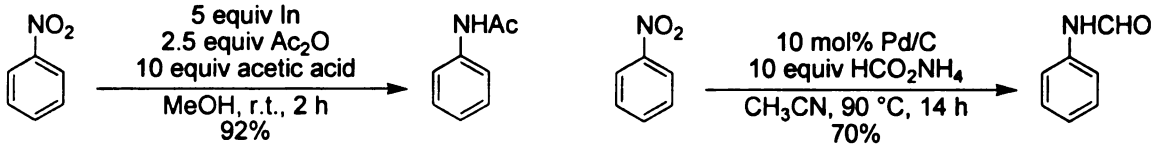
The use of silanes and siloxanes for the reduction of nitro groups has somewhat surprisingly been ignored,[97] with only a hand full of examples in the literature. During the 1970's, Andrianov and co-workers[98] used several silanes for nitroarene reductions, but incomplete reactions and low yields were their norm. During this same period, Lipowitz and Bowman reported a single Pd/C catalyzed reduction of nitrobenzene by polymethylhydrosiloxane (PMHS). To the best of our knowledge, the only other example where PMHS is used in such a capacity[99] is a report by Blum and Vollhardt,[100] that states that nitrobenzene was reduced to aniline by a rhodium catalyst under transfer hydrogenation. Two decades later, Brinkman and Miles[101] demonstrated that Wilkinson's catalyst and triethylsilane promotes the reduction of nitrobenzenes, with moderate functional group compatibility (Scheme 21).

Scheme 21. Previous Examples of Nitroarene Reductions Using Silyl Hydrides



Despite the large number of methods that have been developed for the reduction of nitro groups, only a few methods follow the reduction with subsequent chemical events. This is unfortunate, for there is an ever-growing need to develop greener methodology that allows multiple reactions to be run one-pot. Of the procedures already created, the amine intermediate can be alkylated,[102] transformed to amides[103] or carbamates,[104] and be used to form heterocycles[105] or heteroaromatics.[106] The methods that have been developed for reductive transformation of nitro groups to amides are limited to the synthesis of acet- and formamides[107] (Scheme 22). The reductive transformation of nitro groups is relatively unexplored, and a system has yet been developed that can synthesize a variety of amides from the corresponding nitro compounds.

Scheme 22. Reductive Transformation of Nitro Groups to Acet- and Formanides[103,107]

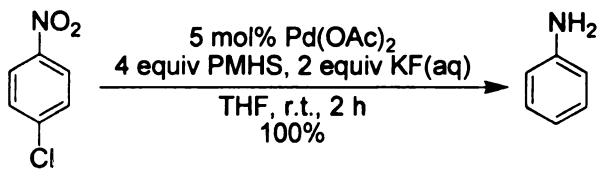


Exploration into reduction methods was born out of our group's interest in synthesizing organotin hydrides with PMHS. The in situ reduction of organotin halides to organotin hydrides by fluoride activated PMHS was applied to a number of classical tin reactions.[5] Furthermore in situ preparation of vinylstannanes via the initial reduction of the organotin halides, was extended to a one-pot hydrostannation/Stille coupling catalytic in tin. The aforementioned chemistry led to the discovery that a combination of catalytic $Pd(OAc)_2$, PMHS, and aqueous KF creates a versatile and mild reducing method. The combination of these reagents can efficiently and mildly hydrodehalogenate aryl chlorides,

allow for 1,4-reduction of enones,[108] and facilitate the reductive cleavage of benzylic C-O bonds,[109] all at room temperature. The reactivity of this reduction system is likely due in part to the formation of palladium nanoparticles, as recognized by Chauhan.

While screening substrates in our chlorodehalogenation system [$Pd(OAc)_2$/PMHS/KF] (Chapter 3), we found that 1-chloro-4-nitrobenzene was quantitatively transformed to aniline (Scheme 23). Given this result, the limited nature of prior work utilizing silicon hydrides, and the advantages associated with PMHS (low toxicity and cost, air and moisture stable, high functional group tolerance) and related silyl hydrides, warranted a full study on nitro reductions using $Pd(OAc)_2$/PMHS/KF.

Scheme 23. Discovery of $Pd(OAc)_2$/PMHS/KF Nitro Reduction



5.2 Optimization of the Reaction Conditions for Nitroarene Reduction

To test the generality of this system for nitro group reduction,[110] we simply subjected nitrobenzene to our dehalogenation conditions, which gratifyingly afforded aniline in quantitative yield, with a reaction time of less than 30 minutes. To build from this result, the reduction of 2-nitrotoluene was screened against a variety of palladium and fluoride sources, solvents, and siloxanes/silanes. In the absence of a palladium catalyst, in the presence of 2 equivalents of PMHS and KF(aq), no amine formation was seen after 1 day. With the necessity of palladium established, a number of catalysts were tested, of which, $Pd(OAc)_2$

(70%) was found to be the most efficient (Pd/C (62%), $PdCl_2$ (59%), Pd_2dba_3 (55%)). In contrast, added Ph_3P or the use of phosphine-bearing catalysts shut the reduction down. $Pd(OAc)_2$ was selected for further optimization studies owing to its higher reduction efficiency, relatively low cost, and previously noted functional group tolerance.

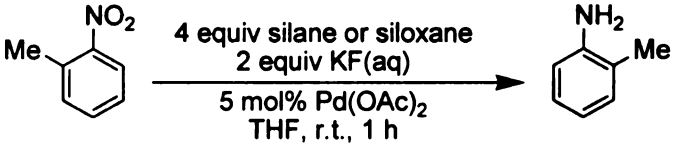
To establish the importance of fluoride in the reduction, the reaction of 2-nitrotoluene was run fluoride free, in the presence of 5 mol% $Pd(OAc)_2$ and 4 equivalents PMHS. Under such conditions, no amine product was observed after 1 h, but at 24 h 2-aminotoluene was obtained in 50% yield. Presumably, fluoride aids formation of polycoordinate siloxane intermediates, allowing for facile transfer of the hydride. In this role, most simple anhydrous alkaline fluoride salts (LiF, NaF, KF, CsF) proved equally effective, along with potassium fluoride dihydrate. TBAF could also be employed, but only when used in substoichiometric amounts (10 mol%) and under cryogenic (-78 °C) conditions. Use of 1 equivalent of TBAF at –78 °C or in any amount at room temperature caused the reaction mixtures to turn into a solid mass via sol-gel formation.

Reaction efficiency was dramatically affected by choice of reaction solvent. Reduction of 2-nitrotoluene with 5 mol% $Pd(OAc)_2$, 2 equivalents PMHS, and 2 equivalents of KF(aq) in THF and EtOAc gave the highest yields (70% and 67%, respectively) of the amine, whereas 1,4-dioxane (24%), benzene (31%), hexanes (17%), CH_2Cl_2 (33%), and CH_3CN (30%) were poor reaction media, and only starting material being recovered when run in DMF or NMP.

Perhaps most surprisingly, was that precipitation of the catalyst and gel formation upon prolonged stirring was observed in Et_2O.

Nearly all silanes and siloxanes screened (Table 15) were able to efficiently reduce 2-nitrotoluene to 2-aminotoluene with the $Pd(OAc)_2$/KF(aq)/THF combination. Nonetheless, PMHS remained the silyl hydride of choice. A byproduct of the silicone industry, PMHS is inexpensive and tends to be much more air and moisture stable than other siloxanes.[111] Indeed, PMHS can be stored on the bench for long periods of time (years) and no extraordinary measures are needed when measuring out or using this reagent.

Table 15. Silane/Siloxane Screening in Reduction of 2-Nitrotoluene



Entry	Silicon Hydride	% Yield[a]
1	PMHS	100
2	Et_3SiH	100
3	TMS_3SiH	23
4	$EtO(Me)_2SiH$	100
5	$TMSO(Me)_2SiH$	100
6	$Me(MeO)_2SiH$	97
7	$Me(TMSO)_2SiH$	90
8	$(TMSO)_3SiH$	0
9	1,3-bis(trimethylsiloxy)-1,3-dimethyldisiloxane	100
10	methylhydrocyclosiloxanes	30

a) Determined by ^1H NMR with an internal standard (CH_2Cl_2), average of two runs.

5.3 Reduction of Aromatic Nitro Groups to Amines with the $Pd(OAc)_2$/PMHS/KF System

Thus, after much investigation, our optimal conditions were determined to be the first conditions examined, namely, 5 mol% of $Pd(OAc)_2$, 4 equivalents of PMHS, and 2 equivalents of aqueous KF in THF at room temperature. Substrate screening of a variety of nitro-substituted arenes and heteroarenes was thus

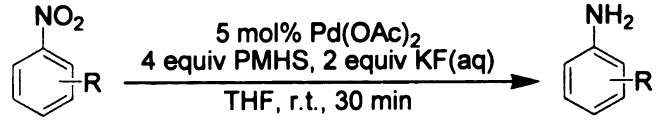
initiated (Tables 16-19). In practice, the reaction system tolerated substituents irrespective of their ring position. The steric hindrance of one ortho functional group did not affect reaction times, but in the case of 2-nitro-*m*-xylene (Table 16, entry 3), with two functional groups ortho to the nitro group, the reaction time was considerably slower (180 vs 30 min). Electron-donating functional groups were well tolerated with quantitative formation of the corresponding anilines typically observed (Table 16, entries 4-9, 11-13). One exception to this rule was 4-nitrothioanisole, which gave a complex mixture of products containing ~10% of the expected amine (Table 16, entry 10). Since sulfur is a well-known Pd scavenger and poison, we assume this was a factor in that negative result. In terms of electron-withdrawing functional groups the system tolerated carboxylic acids (Table 16, entry 19), esters (Table 16, entries 16-18, 24), amide (Table 16, entry 20 and 24), and trifluorotoluene (Table 16, entry 25). Adjustment of the PMHS concentration to 3-3.5 equivalents allowed selective reduction of a nitro in the presence of a benzylic ketone (Table 16, entry 27-28), but the use of 4 equivalents of PMHS reduction of the benzylic ketone occurs after complete reduction of the nitro group. Reduction of the nitro group was favored with 4-nitrobenzaldehyde affording the aniline in 73% yield (Table 16, entry 26), but intrusive reduction of the aldehyde to the alcohol (24%) was unavoidable (reductive amination was not witnessed). Again, reactions were typically complete within 30 min, with formation of the amino-substituted benzonitriles being notable exceptions (Table 16, entries 21-23). For these substrates 12 h reaction times were necessary, unless KF concentrations were increased. With

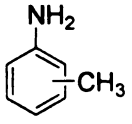
4 equivalents of KF the 2- and 3-nitrobenzonitriles could be quantitatively reduced to their aniline derivatives within 4 hours. However, even under these more forcing conditions 4-nitrobenzonitrile could only be partially reduced to the *N*-hydroxylamine (entry 23). The sluggish reactivity of this substrate may be attributable to increased resonance stabilization of its intermediates.

In addition to the functional group tolerances mentioned above, it should be noted that despite the presence of KF the TBS-protected aminophenol (entry 13) was isolated in high yield accompanied by only 7% of the desilylated phenol. This was not the case with 1-(benzyloxy)-4-nitrobenzene where debenzylation of the protected phenol was the major reduction pathway, affording the benzyl-protected aminophenol in only 27% yield (entry 14). A nitro group could be selectively reduced to the amine in the presence of a less activated benzyl ether (entry 15). Chemoselective nitro reductions were not achieved in the presence of an aromatic bromide of chloride. On the other hand aromatic fluorides were not dehalogenated under these conditions (entries 30-32). In the case of an aliphatic bromide (entry 33), nitro reduction was favored over dehalogenation, but unconsumed PMHS after reduction of the nitro group promoted the dehalogenation of the aliphatic bromide. With 4 equivalents of PMHS full reduction of the nitro group to the amine was accomplished, but 15% dehalogenation was also observed. Simply adjusting the PMHS concentration to 3.5 equivalents allowed for exclusive reduction of the nitro group.

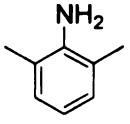
The system tolerated an electron-donating and withdrawing group on the arene (entries 35-37), affording the aniline product in near quantitative yield.

Table 16. Anilines Formed by the Reduction of Nitroarenes with $Pd(OAc)_2$/PMHS/KF

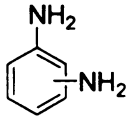




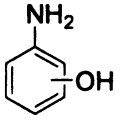
(1) *ortho* - 94%
(2) *para* - 94%



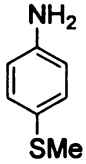
(3) 100%



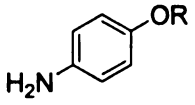
(4) *ortho* - 97%[d]
(5) *meta* - 99%
(6) *para* - 95%



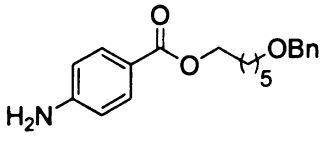
(7) *ortho* - 98%[d]
(8) *meta* - 93%
(9) *para* - 97%[d]



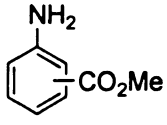
(10) ~10%



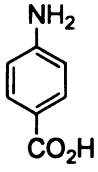
(11) R = Me 98%
(12) R = Ac 94%
(13) R = OTBS 92%[b]
(14) R = OBn 27%



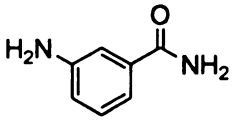
(15) 100%



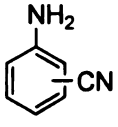
(16) *ortho* - 100%
(17) *meta* - 100%
(18) *para* - 100%



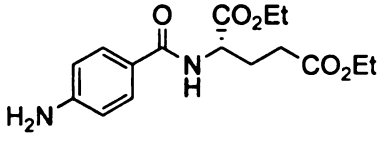
(19) 94%[e]



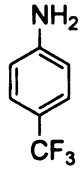
(20) 92%



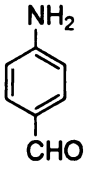
(21) *ortho* - 97%[f]
(22) *meta* - 98%[f]
(23) *para* - 77%[fi]



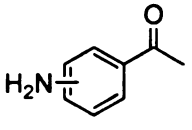
(24) 100%



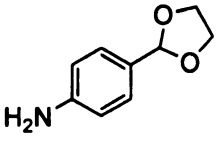
(25) 99%



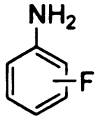
(26) 73%[bj]



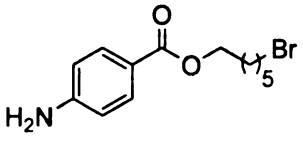
(27) *meta* - 97%[c]
(28) *para* - 95%[b]



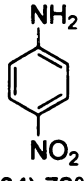
(29) 80%



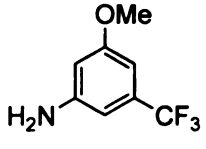
(30) *ortho* - 97%
(31) *meta* - 96%
(32) *para* - 97%



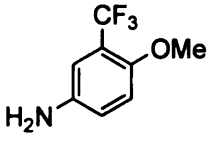
(33) 100%[c]



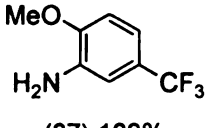
(34) 72%[k]



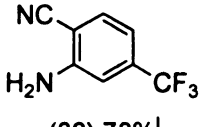
(35) 99%[g]



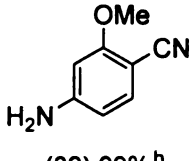
(36) 98%



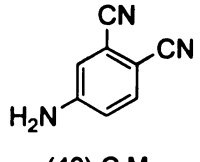
(37) 100%



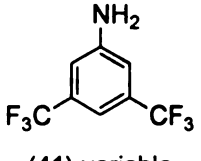
(38) 78%[l]



(39) 99%[h]



(40) C.M.



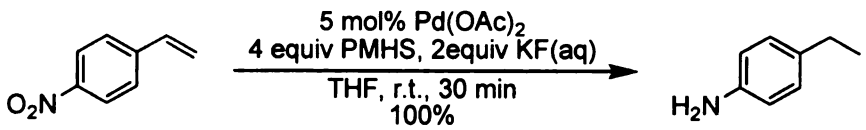
(41) variable

a) Isolated yields after flash chromatography b) run with 3 equiv PMHS c) run with 3.5 equiv PMHS d) Isolated as the acetamide e) Isolataed as acetylamino benzoic acid f) stirred for 12 h or 4 h with 4 equiv KF g) stirred for 12 h h) stirred for 1 h i) represents 4-(*N*-hydroxylamino)-benzonitrile j) 24% (4-nitrophenyl)methanol k) 20% 1,4-diamine l) 20% 2-amino-4-trifluoromethyl-benzamide

Even though the nitrobenzonitriles required prolonged reaction times, 2-nitro-4-(trifluoromethyl)benzonitrile (entry 38) was reduced in the prototypical reaction time of 30 min, accompanied by 20% hydrolysis of the nitrile to the amide. Anderson[112,113] reported in a patent that 2-nitro-4-(trifluoromethyl)benzonitrile is reduced and hydrolyzed completely to 2-amino-4-(trifluoromethyl)benzamide, with standard palladium hydrogenolysis conditions (Pd/C, H_2, MeOH, rt). What should be noted is that under our system only 20% amide formation occurs. The addition of a methoxy group on a nitrobenzonitrile (entry 39) reduced the reaction time back to the 30 minutes yielding the *N*-hydroxylamine, and quantitatively affording the amine at 1 hour. The reaction of 4-nitrophthalonitrile, gave a complex mixture of products after 30 minutes (entry 40). Complete consumption of starting material occurred for 1-nitro-3,5-bis(trifluoromethyl)benzene (entry 41), but the reaction was inconsistent affording varying ratios of *N*-hydroxylamine and amine for each run.

5.3.1 Establishing the Systems Tolerance for Olefins and Alkynes

Scheme 24. Over Reduction of 4-Nitrostyrene



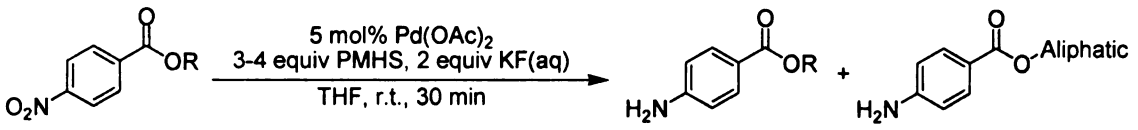
Subjection of 4-nitrostyrene to the reaction conditions produced 4-ethylaniline quantitatively (Scheme 24). This result was not unexpected, for there are known literature examples were PMHS and a transition metal have been used for the reduction of alkenes and alkynes.[1,100] We had also already determined that the $Pd(OAc)_2$/PMHS/KF system is capable of reducing activated

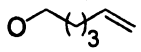
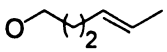
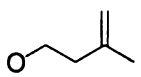
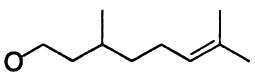
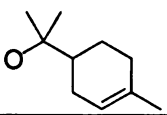
olefins and alkynes, and 1,4-reduction of enones.[108,109] The question we sought to answer, was would the system tolerate unactivated olefins and alkynes (Table 17 and Scheme 25)? So a variety of unactivated mono-, di-, and tri-substituted olefins were prepared from 4-nitrobenzoic acid and the corresponding alcohol. Reduction of the nitro-aromatic was only slightly favored over the mono-substituted olefin, yielding the aniline mono-olefin in a low 27% yield (entry 2). The yield of the desired product was increased for an internal di-substituted olefin to 51% (entry 3), and 60-64% for an external di-substituted olefin, which also had 13-20% isomerization of the double bond to the more thermodynamically stable tri-substituted olefin (entries 5-7). Adjustment of the PMHS concentration to 3.5 equivalents for the tri-substituted olefins produced the desired aniline olefins in 90% and 93% yield (entries 9 and 11). However, reduction of the double bond could not be completely stopped with 4% and 7% over reduced material always being observed. Reduction of a TBS-protected alkyne to the vinyl silane is selective over nitro reduction, after which point nitro group reduction to the amine is favored. Here too isomerization and reduction of the vinyl silane double bond occurs. Reduction of the alkyne, and isomerization of the vinyl silane is assumed to occur via a palladium mediated hydrogenation mechanism.[114] Increasing the PMHS concentration to 6 equivalents efficiently reduced both the nitro group to the amine and the alkyne to the saturated hydrocarbon (Scheme 25).

5.3.2 Reduction of Dinitroarenes

Attempted monoreduction of 1,4-dinitrobenzene afforded 4-nitroaniline (Table 18, entry 2) in 72% yield along with 20% of the diamine. A similar result was seen

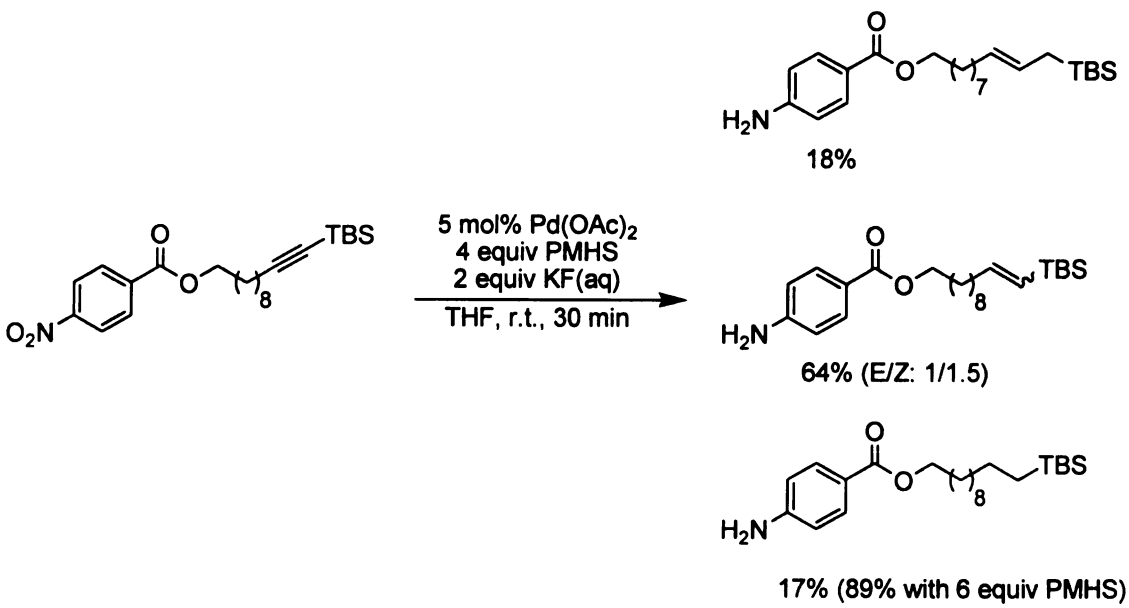
Table 17. Determining the Tolerance of Unactivated Olefins



Entry	OR	equiv PMHS	%Yield[a]	%Yield[a] Reduced Olefin
1		3	19	55
2		4	27	73
3		3	51	22
4		4	41	54
5		3	60 (13)	10
6		3.5	64 (18)	15
7		4	60 (20)	19
8		3	75	1
9		3.5	90	4
10		4	68	32
11		3.5	93	7
12		4	49	50

a) Isolated yields after flash chromatography
( ) %yield of isomerized double bond to tri-substituted olefin

Scheme 25. Testing the Compatibility of an Unactivated Alkynes



with bis(4-nitrophenyl)-methane, where doubling the PMHS and KF concentrations gave diamine in high yield after 30 min (Table 18, entries 3-5). Mono-reduction of 1-methoxy-2,4-dinitrobenzene occurs in 69% yield, with no selectivity for either nitro group. The diamine was afforded in good yield after doubling the PMHS and KF concentrations (entries 6-7). As seen previously, the presence of a nitrile proved to be capricious, with all starting material being consumed but only a complex mixture of products being afforded (entries 8-9).

Table 18. Reduction of Dinitro-arenes[a]

Entry	Starting Material	Equiv PMHS	Equiv KF	%Yield Mono-amine	%Yield Di-amine
1	1,4-dinitrobenzene	3	2	44	0
2		4	2	72	20
3	Bis(4-nitrophenyl)methane	3	2	48	30
4		6	4	17	83
5		8	4	0	93
6	1-methoxy-2,4-dinitrobenzene	4	2	69 (1/1)	0
7		8	4	0	89
8	2,4-dinitrobenzonitrile	4	2	CM	CM
9		8	4	CM	CM

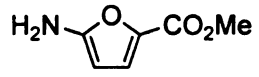
a) Conditions: 1 mmol dinitroarene, 5 mol% $Pd(OAc)_2$, PMHS, KF, 5 mL THF, 2 mL H_2O, rt, 30 min b) Isolated yields after flash chromatography CM = complex mixture

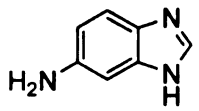
5.4 Reduction of Nitro-Heteroaromatics to Amines

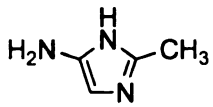
Extension of the methodology to nitro-substituted heteroaromatics afforded the expected amines in high yields, but not without some nuances. Our standard procedure, where PMHS is added last, produced an atypical color change and only afforded starting material for 5-nitrobenzimidazole. We hypothesized that formation of the active Pd-PMHS complex was hindered by coordination of the substrate to the metal. To overcome this problem, we simply premixed the reagents, so as to allow nanoparticle formation in advance of exposure to 5-nitrobenzimidazole. This protocol, where the substrate was added after nanoparticle formation, gave the expected amine in high yield (Table 19,

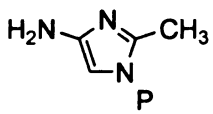
entry 2). Application of the modified protocol to 2-methyl-4(5)nitroimidazole (entry 3) resulted in complete consumption of all of the starting material, but only a complex mixture of products was isolated. Attempts to inhibit decomposition of the desired amine by protection/derivatization of the imidazoles (protecting groups = Ac, Bn, CH_2CH_2CN) was partially successful (entry 4). Unfortunately the amine product could not be isolated clean. A pyrazole on the other hand was tolerated with out incidence (Table 19, entry 5). In contrast to the aforementioned heterocycles, the standard conditions were capable of reducing a nitro group in the presence of a pyridine in quantitative yield (entries 6-8) and methyl 5-nitro-2-furanoate in 89% yield (Table 19, entry 1). Whereas 4-nitrothioanisole (Table 16, entry 10) was a problem substrate, sulfur atoms in the aromatic ring do not uniformly inhibit the nitro reduction. Nitro reduction occurred in moderate to good yield for substrates containing a thioimidazole (Table 19, entries 9-10), and 2-nitrothiophene was also easily reduced to the amine (Table 19, entry 12); however, isolation of the product was difficult and could only be achieved after its in situ protection as a Boc carbamate. As was the case with the imidazoles, a nitro group could be reduced in the presence of a 1,2,3-thiadiazole (Table 19, entry 11), but only a complex mixture of products was afforded.

Table 19. Reduction of Nitro-Substituted Heteroaromatics[a]

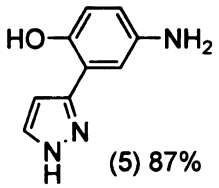

(1) 89%

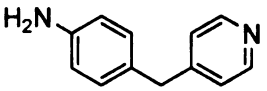

(2) 89%

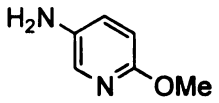

(3) CM

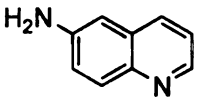

P = Ac, Bn, CH_2CH_2CN

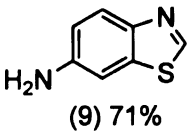
(4) CM

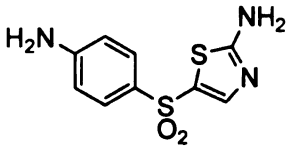

(5) 87%

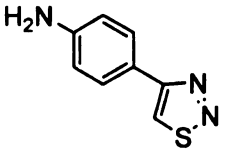

(6) 99%

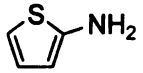

(7) 100%


(8) 99%


(9) 71%


(10) 94%


(11) CM


(12) 81%

a) Conditions: nitroheteroaromatic (1 mmol), $Pd(OAc)_2$ (0.05 mmol), PMHS (4 mmol), KF (2 mmol), THF (5 mL), degassed H_2O (2 mL), room temperature. b) Isolated yields after flash chromatography c) Isolated as acetamide d) Isolated as Boc protected amine

5.5 Reduction of Aliphatic Nitro Groups to *N*-Hydroxylamines via a Simple Modification of the System

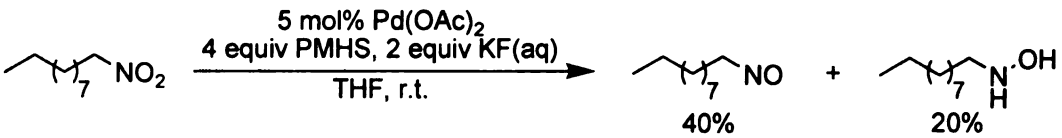
5.5.1 Discovery and Development of *N*-Hydroxylamine Synthesis from Aliphatic Nitro Groups with Palladium Nanoparticles

At this point, we became interested in applying this system to the reduction of aliphatic nitro compounds, to the corresponding amines. Our first attempt met with little success. Subjection of 1-nitrodecane to the conditions (Scheme 26) yielded none of the aliphatic amine, a small amount of *N*-hydroxyl-1-aminodecane (15-20%), the corresponding nitroso compound (40%), and unreacted starting material (23%). Even though none of the desired aliphatic

amine was formed, a small amount of the *N*-hydroxylamine was, which could be capitalized on.

N-Hydroxylamines are important components in the synthesis of nitrones,[90,115] Bode and co-workers have utilized them in a decarboxylative condensation with α-ketoacids for the formation of amides,[116] and they are found in natural products and biologically active compounds. Unfortunately only a handful of methods have been developed for the synthesis of *N*-hydroxylamines from aliphatic nitro compounds.[90,95,117] These methods tend to have low functional group compatibility, require harsh reaction conditions, or are low yielding. The opposite approach to the synthesis of *N*-hydroxylamines can be taken, via the oxidation of aliphatic amines, but this route is also fraught with problems.[90,117] Thus we sought to expand our $Pd(OAc)_2$/PMHS/KF system to include aliphatic *N*-hydroxylamines from the corresponding nitro compound.

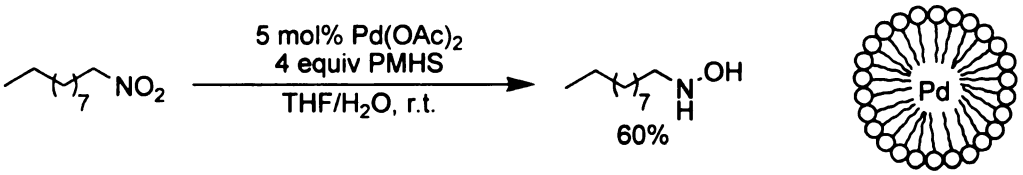
Scheme 26. Attempted Synthesis of an Aliphatic Amine with the $Pd(OAc)_2$/PMHS/KF System



Utilizing 1-nitrodecane as the test substrate, adjustments to the catalyst loading, PMHS concentration, fluoride source, and temperature afforded small increases in the *N*-hydroxyl-1-aminodecane yield, but not at levels that were synthetically useful. The low yields were attributed to a competing side reaction consuming the hydride, for the slower reacting aliphatic nitro compounds. To overcome this side reaction it was conjectured that simply removing the fluoride source would decrease the reactivity of the silyl hydride, there by increasing the

yield of the hydroxylamine. This theory was found to be correct. By running the reaction in the absence of KF a ~60 conversion to the *N*-hydroxylamine was seen (Scheme 27). Complete conversion did not occur because concomitant sol-gel formation also took place, encapsulating the catalyst and shutting the reaction down. A potential solution to this problem would be to simply swap PMHS for a non-polymeric silicon hydride.

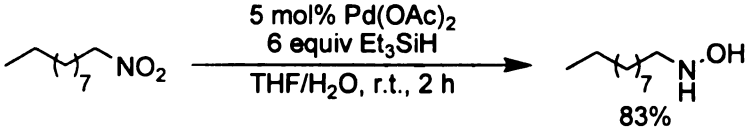
Scheme 27. Suppression of Side-Reaction by Elimination of Fluoride Source



Sol-gel Encapsulated Catalyst

Through our initial optimization studies a number of non-polymeric silanes and siloxanes had already been determined to work (Table 15). Rescreening these silane and siloxanes in the reduction of the nitroalkane revealed triethylsilane as the best choice, converting 85% of 1-nitrodecane to *N*-hydroxyl-1-aminodecane in 2 h. It should be noted, that even though the fluoride source was removed, the addition of water remained critical to the reaction's success as anhydrous conditions gave low product yields. Also, to ensure complete consumption of the nitroalkane with reproducible yields, six equivalents of triethylsilane need to be used (Scheme 28).

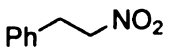
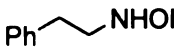
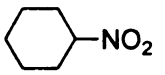
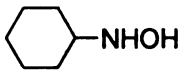
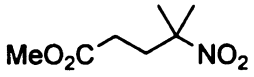
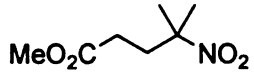
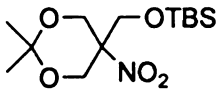
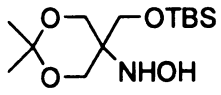
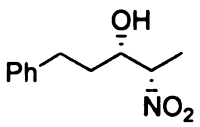
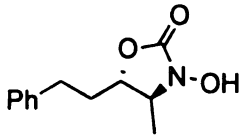
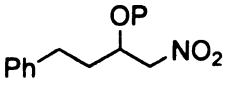
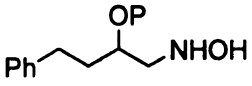
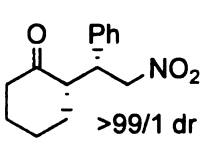
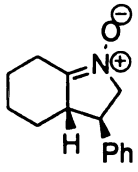
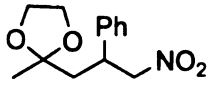
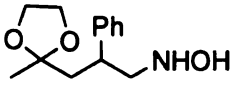
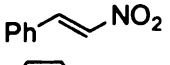
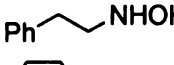
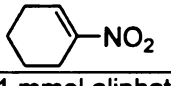
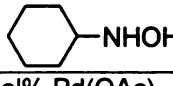
Scheme 28. Conditions Determined For Reduction of Aliphatic Nitro Groups



5.5.2 Substrate Screening of Nitro Aliphatics

Determining the conditions necessary for reduction of aliphatic nitro groups to be 5 mol% $Pd(OAc)_2$, 6 equivalents Et_3SiH, in THF/H_2O, a screening of aliphatic nitro compounds was initiated (Table 20). Primary and secondary nitro groups responded favorably, being efficiently reduced within 2 h. However, this was not the case for tertiary nitro aliphatics, which reacted poorly. Reduction of the highly oxygenated 1,3-diacetoxy-2-acetoxymethyl-2-nitropropane was only modestly successful with a 31% yield of the *N*-hydroxylamine (Table 20, entry 4) being realized. Only trace amounts of the desired product could be isolated from methyl 4-methyl-4-nitropentanoate, with 64% recovery of the starting material (entry 5). Despite the fact that only trace amounts of the hydroxylamine was isolated, it is possible that ~36% (based on recovered S.M., 64%) of the hydroxylamine was formed, then cyclized to the *N*-hydroxylactam, which was unstable and decomposed. This may also be the case with the tertiary nitroacetonide (entry 6), where the newly formed hydroxylamine decomposed when exposed to the reaction conditions. A Henry adduct, prepared diastereoselectively, afforded the reduction product in high yield with complete retention of the stereochemistry. Irrespective of protecting group (entries 8-15), protected Henry adducts (TES, TBS, Ac, Me) proved less efficient, consistently yielded the hydroxylamine in a diminished 44-56% yield. Increasing the triethylsilane concentration to 10 equivalents produced only a ~10% increase in product yield, 54-57%, with the exception of the Me protected alcohol where the hydoxylamine was produced in 84%.

Table 20. Reduction of Aliphatic Nitro Compounds to *N*-hydroxylamines with $Pd(OAc)_2/Et_3SiH$ in a THF/H_2O mixture[a]

Entry	Aliphatic Nitro	*N*-Hydroxylamine	Equiv Et_3SiH	%Yield[b]
1			6	83
2			6	58
3[c]			6	89
4	$(AcOCH_2)_3C-NO_2$	$(AcOCH_2)_3C-NHOH$	6	31 (66% SM)
5			6	>1 (64% SM)
6			6	0 (77% SM)
7[d]	 1.8/1 syn/anti	 1.8/1 anti/syn	6	82
				
8	P = TES	P = TES	6	44
9			10	56
10	P = TBS	P = TBS	6	45
11			10	57
12	P = Ac	P = Ac	6	49
13			10	54
14	P = Me	P = Me	6	56
15			10	84
16			6	39 (37% SM)
17			10	77 (19% SM)
18			12	45 (10% SM)
19	>99/1 dr		10 + 0.25 eq KF	67 (0% SM)
20			6	51
21			8	53
22[c]			8	88

a) Conditions: 1 mmol aliphatic nitro, 5 mol% $Pd(OAc)_2$, PMHS, THF/H_2O (5/2 mL), rt, 2-4 h
b) Isolated yields after flash chromatography c) Isolated as *N*-hydroxyl-sulfonamide
d) 2 equiv $Imid_2CO$ added after complete consumption of SM and stirred for 6 h

We also found that subsequent chemical events, intra- or intermolecular trapping with an electrophile could follow the nitro reduction. The Henry adduct hydroxylamine was trapped with 1,1'-carbonyldiimidazole and transformed into a *N*-hydroxyl-oxazolidinone (entry 7). A Michael adduct, prepared stereoselectively, underwent a Reissig nitrone synthesis,[118] where the intermediate hydroxylamine condensates with the ketone, forming the cyclic nitrone with no loss of stereochemistry (entries 16-19). The optimal yield of 77% was achieved with 10 equivalents Et_3SiH. Increasing the Et_3SiH to 12 equivalents decreased the yield of the nitrone. Starting material was recovered from the reduction of the Michael adduct when using 6-12 equivalent of the Et_3SiH. In an attempt to force the reaction to consume all of the Michael adduct, the reduction was run with a catalytic amount of KF (0.25 equivalents). The addition of catalytic KF did result in full consumption of the starting material, regrettable this also caused the yield of the nitrone to decrease. These negative returns for the Michael adduct are attributed to the system reducing the nitrone when using 12 equivalents of Et_3SiH, or catalytic amounts of KF. Protection of the Michael adduct ketone, as the ketal, did not inhibit the reduction process (entry 20). Using 8 equivalents of triethylsilane allowed vinylnitro compounds to be efficiently reduced to the primary and secondary *N*-hydroxylamimes (entries 21-22).

5.6 Adjustment of the Catalyst Loading

Depending on the desired application the use of 5 mol% $Pd(OAc)_2$ may be to large, for that reason the catalyst loading was systematically decreased while

screening against a variety of aromatic nitro compounds (Table 21). Lowering the catalyst loading to 1 mol% increased the reaction time to 3 hours for the aromatic substrates with no loss in product yield, as was the case with 0.5 mol% $Pd(OAc)_2$ (15 hour reaction times). Diminishing returns set in when decreasing the catalyst loading to 0.1 mol%, where the reduction became substrate dependent, working well only for methyl 4-nitrobenzoate. Simultaneously decreasing the catalyst loading to 0.5 mol%, and increasing the size of the reaction to 45 mmol had no effect on the reaction efficiency, affording the amine products in the same yields when run with 5 mol% $Pd(OAc)_2$ on a 1 mmol scale.

Table 21. Determining the Lowest Usable $Pd(OAc)_2$ Concentration

Substrate	mol% $Pd(OAc)_2$ / (Time-hours)			
	5 / (0.5)	1 / (3)	0.5 / (15)	0.1 / (48)
methyl 4-nitrobenzoate	100	100	92	100
4-nitroanisole	98	94	98	51
methyl 5-nitro-2-furoate	89	90	91	CM

Conditions: Nitroarene (1 mmol), $Pd(OAc)_2$, PMHS (4 mmol), KF (2 mmol), THF (5 mL), degassed H_2O (2 mL), r.t.

5.7 Proposed Mechanism

Our findings and previous work done with the palladium-PMHS nanoparticles have led us to surmise the nitro group reduction to advance via the nitroso and then hydroxylamine intermediates/products. The precise mechanism by which these intermediates are formed and subsequently reduced is not entirely clear. The presence of water has a dramatic influence on reaction efficiency and rate. This is attributed to a transfer hydrogenation process where hydrogen gas is formed on the palladium via a σ bond metathesis between the silicon hydride and water. So reduction of the nitro group to the nitroso is most likely occurring through hydrogenolysis. Based on past literature precedent[119]

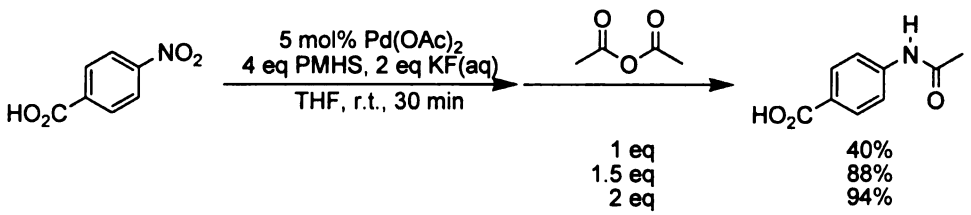
the nitro group could also be oxidizing a silicon coordinated to the palladium, resulting in nitroso formation. To evaluate this pathway nitrobenzene was subjected to reaction conditions using $Pd(OAc)_2$, PMHS, and anhydrous THF, which resulted in the reaction mixture turning into one solid mass via sol-gel formation. Swapping PMHS with triethylsilane eliminated sol-gel formation, an indicated the formation of *N*-phenyl-*O*-(triethylsilyl)hydroxylamine by NMR of the crude reaction mixture. This result gives credence to the oxidation pathway, but under the aqueous reaction conditions hydrogenolysis is assumed to be the major reduction mechanism. Three potential pathways for reduction of the nitroso to the hydroxylamine are (1) hydrogenolysis, (2) palladium catalyzed hydrosilylation, or (3) fluoride catalyzed hydrosilylation. Based on the result of the aforementioned control reaction and intermediates isolated with the aliphatic substrates, reduction of the nitroso appears to take place by hydrogenolysis and hydrosilylation. Reduction of the hydroxylamine is most probably occurring through hydrogenolysis alone.

5.8 A One-Pot Reductive Conversion to Amides, Sulfonamides and Carbamates

It became necessary with 4-nitrobenzoic acid and 2-nitrothiophene to derivatize the amine product so isolation of the material could be accomplished. For this reason, we asked if the amine products could be trapped with an appropriate electrophile during subsequent chemical events. One of the simplest ways to functionalize an amine is to simply stir it with an anhydride, to form the amide. So 4-nitrobenzoic acid was subjected to the reaction conditions, and at

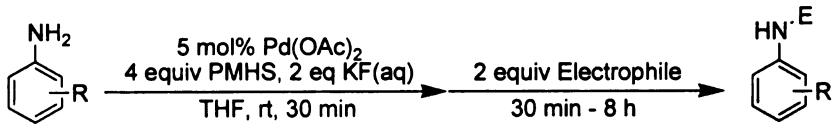
the point TLC indicated that all starting was consumed 1 equivalent of acetic anhydride was added affording 4-acetamidobenzoic acid in 40% yield. The yield of the amide product was doubled when using 1.5 equivalents of acetic anhydride, with full conversion to the amide taking place with 2 equivalents of acetic anhydride (94%) (Scheme 29). Reduction of the nitro group is completely inhibited when the anhydride is added at the beginning of the reduction, with only starting material recovered. Addition of the anhydride to the reaction mixture before complete consumption of the nitroarene halted the reduction at that point, and amide formation was not observed. Reaction success was clearly contingent upon addition of the anhydride after all of the nitroarene had been consumed. Given the every growing need to develop methodology that can be combined with subsequent chemical events, and the lack of established systems that can transform a nitro compound to an amide, we felt further exploration was warranted. This reduction/trapping approach for the synthesis of amides has the advantage that a large selection of aromatic nitro compounds and anhydrides are commercially available.

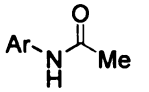
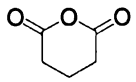
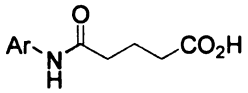
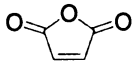
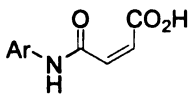
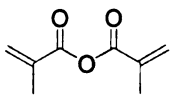
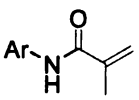
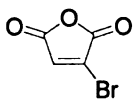
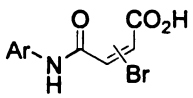
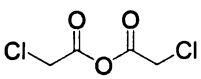
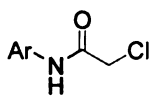
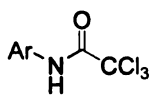
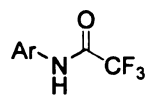
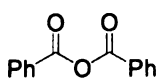
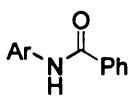
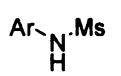
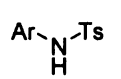
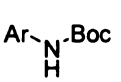
Scheme 29. Evaluating the Feasibility of a One-Pot Reductive Transformation



To determine the generality of this one-pot nitro reduction functionalization, a broad cross-section of anhydrides were tested against

Table 22. One-Pot Reductive Conversion of Nitroarenes to Amides, Carbamates, or Sulfonamides



Entry	Electrophile	Nitroarene	Product	%Yield[a]
1		4-nitroanisole		99
2	Ac_2O	methyl 3-nitrobenzoate		100
3		2-nitro-*m*-xylene		0
4		4-nitroanisole		96
5		methyl 3-nitrobenzoate		87
6		2-nitro-*m*-xylene		0
7		4-nitroanisole		95
8		methyl 3-nitrobenzoate		84
9		2-nitro-*m*-xylene		29
10		4-nitroanisole		99
11		methyl 3-nitrobenzoate		94
12		2-nitro-*m*-xylene		0
13		4-nitroanisole		89 (1/1.3)
14		4-nitroanisole		96
15		methyl 3-nitrobenzoate		84
16		2-nitro-*m*-xylene		<73[b]
17	Trichloroacetic anhydride	4-nitroanisole		0
18	Trifluoroacetic anhydride	4-nitroanisole		0
19		4-nitroanisole		97
20		methyl 3-nitrobenzoate		89
21		2-nitro-*m*-xylene		59
22		4-nitroanisole		79
23	Ms_2O	methyl 3-nitrobenzoate		78
24		2-nitro-*m*-xylene		30
25		4-nitroanisole		97
26	Ts_2O	methyl 3-nitrobenzoate		98
27		2-nitro-*m*-xylene		72
28		4-nitroanisole		98
29	Boc_2O	methyl 3-nitrobenzoate		22
30		2-nitro-*m*-xylene		50

a) Isolated yields after flash chromatography b) amide contaminated with unknown material, yield is based on weight with unknown material.

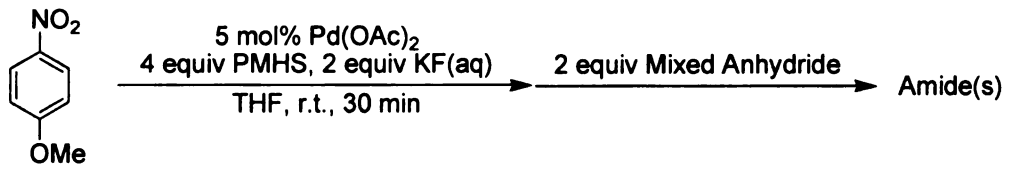
electron rich, electron poor, and sterically congested nitroarenes (Table 22). 4-Nitroanisole performed extremely well, affording the corresponding amides, carbamate, and sulfonamides in high yield (79-99%). An exception to this trend were trichloroacetic and trifluoroacetic anhydrides. Here none of the amide was formed, because the aqueous reaction conditions destroyed the anhydrides upon addition. For that reason these two anhydrides were not tested with the other nitroarenes. Methyl 3-nitrobenzoate also reacted well forming the amides, and sulfonamides in high yield (78-100%), but the carbamate was only produced in 22% yield. The sterics of 2-nitro-*m*-xylene inhibited functionalization of the aniline with yields ranging from 0-72%. Anhydrides containing activated olefins or halides formed the desired amide with out incident, which should be noted, for the $Pd(OAc)_2$/PMHS/KF system typically reduces these functional groups.

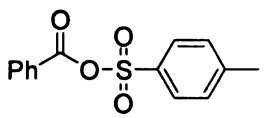
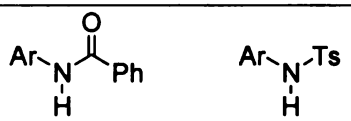
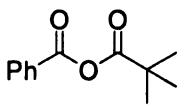
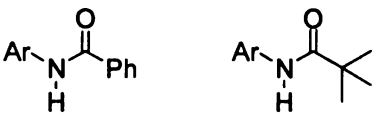
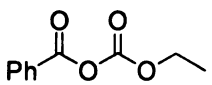
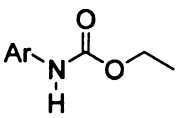
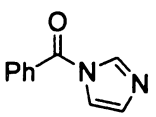
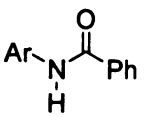
5.8.1 Application of Mixed Anhydrides in Reductive Conversion to Amides

Even though, a large selection of anhydrides are commercially available, the use of mixed anhydrides, prepared form a carboxylic acid, would be useful. To test the practicality of mixed anhydrides with our system, we prepared three of the most commonly used mixed anhydrides from benzoic acid and TsCl, PivCl, and ethyl chloroformate. These mixed anhydrides were tested with 4-nitroanisole (Table 23). The $PhCO_2Ts$ anhydride afforded the amide and sulfonamide in a 1:3 mixture. This was unexpected as the TsO is typically a better leaving group, and there is a known literature example where 4-aminoanisole reacts with $PhCO_2Ts$ selectively producing the benzamide (vide infra). The $PhCO_2Piv$ anhydride also afforded a mixture in a 2:1 ratio, favoring the desired benzamide,

where as the $PhCO_2CO_2Et$ anhydride was completely selective affording the undesired carbamate. A simply solution would be to replace the mixed anhydride with an acid chloride, unfortunately these substrates are more than likely not compatible with the aqueous reaction conditions. However imidazole acetyls are pseudo acid chlorides that are not as water sensitive and that are easily prepared by stirring a carboxylic acid with 1,1-carbonyldiimidazole. The use of 1-benzoylimidazole yielded *N*-(4-methoxyphenyl)benzamide in 75%, demonstrating

Table 23. Screening of Mixed Anhydrides in a One-Pot Synthesis of Amides from a NO_2



Entry	Mixed Anhydride	Amide Product(s) %Yield
1		 25% 75%
2		 67% 33%
3		 100%
4		 74%

a) Isolated yields after flash chromatography

this route as a viable alternative to mixed anhydrides. There was a 22% decrease in product yield, as compared to using benzoic anhydride, but the yield was still sufficiently high enough to warrant exploring this route.

5.8.2 One-Pot Reductive Conversion with Aliphatic Nitro Groups

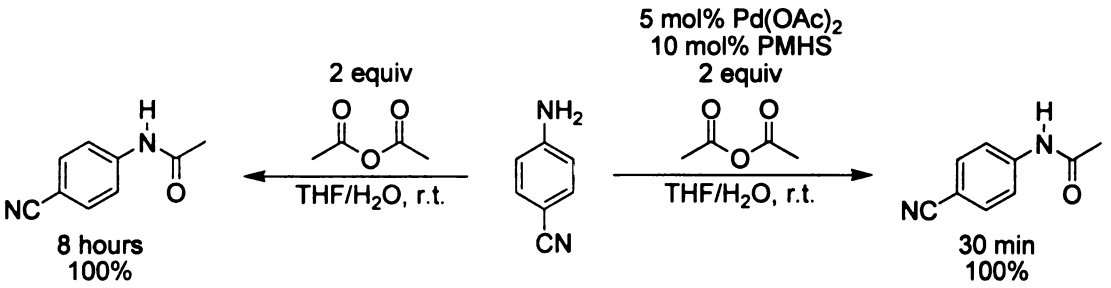
The one-pot functionalization of the nitrogen product was not as successful with the aliphatic hydroxylamines. Typically yields ranged from 0-30%, irrespective of the electrophile used. The one exception being *N*-hydroxyl-cyclohexylamine, where Ts_2O successfully formed the *N*-hydroxyl sulfonamide, in good yield. In all cases tested, none of the hydroxylamine was isolated after addition of the electrophile. It appears that the hydroxylamine intermediates are reacting with the electrophile, but that the *N*-hydroxyl-amide, or -sulfonamide product is not stable under the reaction conditions and/or to flash chromatography.

5.8.3 Role of the Palladium Nanoparticles in the One-Pot Reductive Conversion to Amides, Sulfonamides, and Carbamates

Through the reduction methodology that has been developed using the Pd-PMHS nanoparticles it became apparent that the nanoparticles are electrophilic, more specifically that they are oxophilic with a slight Lewis acidity. It is these characteristics that led us to attempt the one-pot reducutive transformation to amides. Typically the reactions were complete in 30 minutes after addition of the electrophile, which we attributed to the nanoparticles accelerating the amidation. The atypical selectivities seen with the mixed anhydrides can also be attributed to the palladium nanoparticles. A simple

control reaction was run to determine if the nanoparticles are participating in the amidation. First, 2 equivalents of acetic anhydride were added to a round bottom flask containing 4-aminobenzonitrile in a THF/H_2O mixture. The reaction was monitored until complete conversion to the amide occurred (8 h). Next, the Pd-PMHS nanoparticles were preformed in a round bottom flask containing 4-aminobenzonitrile in a THF/H_2O mixture, and 2 equivalents of acetic anhydride were added. Under this set of conditions complete conversion to the amide occurred in 30 minutes, clearly demonstrating that the nanoparticles were accelerating the amidation through activation of the anhydride. The results from the mixed anhydrides can than be explained by the electophilic palladium nanoparticles coordinating to the oxygen with the greatest electron density and activating that segment of the anhydride.

Scheme 30. Control Reaction to Establish if the Nanoparticles Promote the Amidation



5.9 Summary

In summary, nanoparticles formed from $Pd(OAc)_2$ and PMHS, in combination with aqueous KF, rapidly and mildly reduce nitro-substituted arenes and heteroarenes to their corresponding amines in high yields. Substituting PMHS/KF with Et_3SiH, allows for the room-temperature reduction of aliphatic nitro compounds to hydroxylamines. Both variations of the method display good

functional group compatibility and short reaction times. Utilizing the oxo-felicity/Lewis acidity of the palladium nanoparticles the amine products could be transformed to amides, sulfonamides, or carbamates in one pot, by the addition of an electrophile (anhydride) in high yield. Mixed anhydrides were not selective affording a mixture of products, with the exception of $PhCO_2CO_2Et$, which selectively formed the undesired carbamate. The one-pot reductive transformation was not successful with the nitroaliphatics.

Experimental

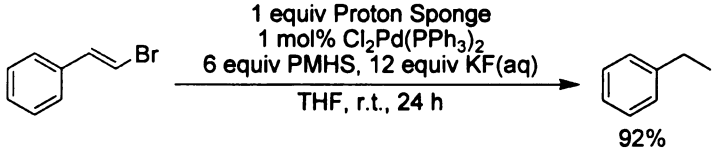
Materials and Methods

All reactions were carried out in oven-dried glassware under an atmosphere of nitrogen, with magnetic stirring, and monitored by thin-layer chromatography with 0.25-mm pre-coated silica gel plates, unless otherwise noted. Tetrahydrofuran was freshly distilled from sodium/benzophenone under nitrogen. Palladium (II) acetate purchased from Strem, anhydrous A.C.S grade potassium fluoride, and polymethylhydrosiloxane (PMHS) purchased from Aldrich were used without purification. Flash chromatography was performed with silica gel 60 A (230-400 mesh) purchased from Silicycle. Yields refer to chromatographically and spectroscopically pure compounds unless other wise stated. Infrared spectra were obtained on a Nicolet IR/42 spectrometer; ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini-300 or a Varian VXP-500 spectrometer (300, 500 MHz for ^{1}H, respectively, and 75, 125 MHz for ^{13}C, respectively), with chemical shifts reported relative to the residue peaks of solvent chloroform (δ 7.24 for ^{1}H and 77.0 for ^{13}C) or dimethyl sulfoxide (δ 2.50 for ^{1}H and 39.5 for ^{13}C). Melting points were measured on a Thomas-Hoover capillary melting point apparatus and are uncorrected; high-resolution mass spectra were obtained at the University of South Carolina, Department of Chemistry and Biochemistry, Mass Spectrometry Laboratory.

Chapter 2 Experimental

General Procedure A

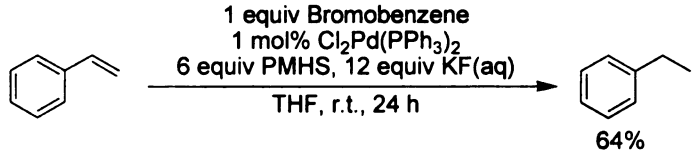
General Procedure for the Dehalogenation of Iodoarenes, Bromoarenes, and α-Bromoketones with $Cl_2Pd(PPh_3)_2$: A round bottom flask was charged with an aryl halide (1mmol), $Cl_2Pd(PPh_3)_2$ (0.01 mmol, 0.007 g), and 5 mL of freshly distilled THF (0.2 M solution). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, an aqueous KF solution (12 mmol, 0.697 g; in 2 mL of degassed H_2O) was introduced by syringe. PMHS (6 mmol, 0.36 mL) was then injected into the reaction mixture. If the reaction mixtures is heated, a reflux condensor is attached to the round bottom and palced 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 were dried over $MgSO_4$, concentrated and subjected to silica gel flash chromatography.



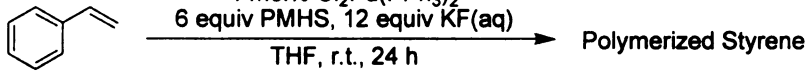
92%

β-Bromostyrene (1 mmol, 0.129 mL) was subjected to general procedure A in the presence of Proton-Sponge® (1 mmol, 0.214 g), and stirred for 24 hours at room temperature. At which point CH_2Cl_2 (1 mmol, 0.064 mL) was injected, and an aliquot (0.1 mL) removed to be examined by ^1H NMR (d1 = 1, nt = 32) to

determine the yield; 5.22 ppm (CH_2Cl_2, set to 2 H), 1.15 ppm (CH_3 for PhEt, measured 2.76 H); 92% ethylbenzene.



Styrene (1 mmol, 0.114 mL) was subjected to general procedure A in the presence of bromobenzene (1 mmol, 0.105 mL), and stirred for 24 hours at room temperature. At which point CH_2Cl_2 (1 mmol, 0.064 mL) was injected, and an aliquot (0.1 mL) removed to be examined by ^1H NMR (d1 = 1, nt = 32) to determine the yield; 5.22 ppm (CH_2Cl_2, set to 2 H), 5.70 ppm (vinyl-H for styrene, measured 0.34 H, 34% S.M.), 1.15 ppm (CH_3 for PhEt, measured 1.95 H); 65% ethylbenzene.



Styrene (1 mmol, 0.114 mL) was subjected to general procedure A in the presence of bromotrimethylsilane (1 mmol, 0.132 mL), and stirred for 24 hours at room temperature. Examination of the reaction mixture by ^1H NMR showed that all of the styrene polymerized.

General Procedure B

General Procedure for the Hydrodehalogenation of Chloroarenes with in situ Formed Palladium-PMHS Nanoparticles [$Pd(OAc)_2$/PMHS/KF]: An oven dried round bottom flask was charged with an aryl chloride (1mmol), $Pd(OAc)_2$ (0.05 mmol, 0.011 g), and 5 mL of freshly distilled THF (0.2 M solution). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, KF (2 mmol, 0.116 g) in 2 mL of degassed water was introduced by syringe. The nitrogen inlet was removed and a balloon of nitrogen was attached. PMHS (4 mmol, 0.24 mL) was then injected dropwise slowly (***Caution**: Rapid addition PMHS can result in uncontrollable gas evolution!*). The reaction was stirred until complete as judged by disappearance on the starting material (GC analysis). The reaction mixture was diluted with Et_2O, the layers separated, and the aqueous layer back extracted with Et_2O. The combined organics were filtered through a plug of Celite (top layer) and neutral alumina (bottom layer) in a 1 cm diameter column by flushing with EtOAc. The crude material was then either distilled or purified by silica gel chromatography. (**Caution**: Reaction is exothermic upon addition of PMHS, so when running on large scale the use of a reflux condenser is recommended.)

Alternate Work Up Procedure I

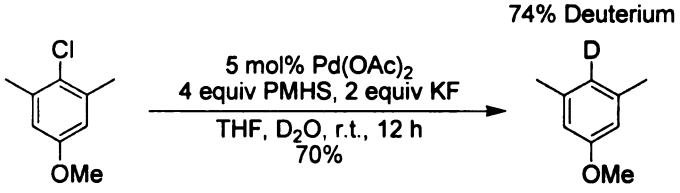
Upon complete reduction, 2 mL of a 3M NaOH solution was added, after stirring for 5 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and

concentrated. The crude material was then either distilled or purified by silica gel chromatography.

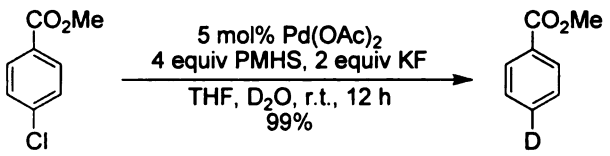
Alternate Work Up Procedure II

Upon complete reduction, the reaction mixture was diluted with 15 mL of EtOAc and TBAF (20 – 50 mol%) was added, the mixture was then stirred for 3 to 6 hours. The layers were separated and the aqueous layer was back extracted with ether. The combined organics were filtered through a plug of neutral alumina or silica gel then concentrated.

Deuterium experiments:



Subjection of 2-chloro-5-methoxy-1,3-dimethylbenzene (1 mmol, 0.170 g) to general procedure B using 2 mL of deuterium oxide (D_2O) afforded 0.096 g (70%) of 1-methoxy-3,5-dimethylbenzene as a clear oil, and unreacted stating material (30%). The percent deuterium incorporation was determined by ^1H NMR; ^1H NMR (300 MHz, $CDCl_3$): δ 6.58 (s, 1H, measured 0.26H, 74% D), 6.51 (s, 2H), 3.75 (s, 3H), 2.27 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.2, 138.7, 136.7, 111.3, 54.7, 20.9. Spectral data were consistent with commercially available non-deuterated material.

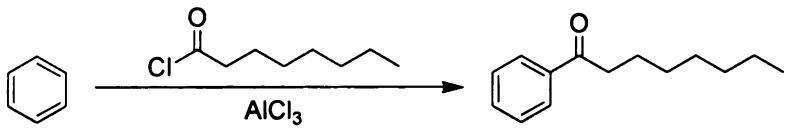


66% Deuterium

Subjection of methyl 4-chlorobenzoate (1 mmol, 0.170 g) to general procedure B using 2 mL of deuterium oxide (D_2O) afforded 0.135 g (99%) of methyl benzoate as a clear oil. The percent deuterium incorporation was determined by ^1H NMR; ^1H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, J = 8.24 Hz, 2H), 7.51 (m, 1H, measured 0.34H, 66% D), 7.40 (m, 2H). Spectral data were consistent with commercially available non-deuterated material.

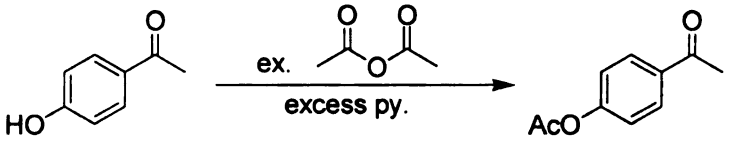
Chapter 4 Experimental

Procedures for the Preparation of Starting Materials Found in Chapter 4

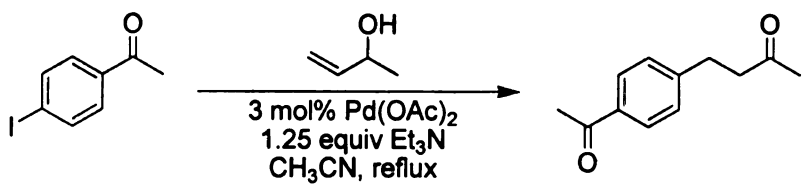


Preparation of 1-phenyl-octan-1-one:[120] a 500 mL three-necked round bottom flask was attached to a reflux condenser and addition funnel, and placed under a positive flow of nitrogen. The r.b. was charged with 1.1 equiv aluminum chloride (220 mmol, 29.3g) and 9.0 equiv of freshly distilled benzene (1800 mmol, 161 mL), and placed in an oil-bath at 75°C. The addition funnel was then charged with octanoyl chloride (200 mmol, 34.1 mL), after heating the benzene mixture for ten minutes the acid chloride was added drop-wise to the solution over an hour. The reaction mixture bubbled vigorously upon addition of the acid chloride. After complete addition of the acid chloride the oil-bath was turned off and the reaction was stirred over night (9 hours). The reaction mixture was poured into an erylmer with 200 mL ice and 50 mL con. HCl. The layers were separated, and the aqueous layer was back extracted with ether. The combined organics were dried over calcium chloride, and concentrated. The crude material was subjected to column chromatography with hexanes / ethyl acetate (90/10) affording 36.49 g (89%) of a light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.94 (d, J = 7.14 Hz, 2H), 7.50 (t, J = 7.14 Hz, 1H), 7.41 (t, J = 7.69 Hz, 2 H), 2.92 (t, J = 7.41 Hz, 2H), 1.70 (quin, J = 7.14 Hz, 2H), 1.26 (m, 8H), 0.85 (t, J = 6.86 Hz, 3H); ^{13}C NMR (75

MHz, $CDCl_3$), δ 200.3, 136.9, 132.7, 128.4, 127.9, 38.4, 31.6, 29.2, 29.0, 24.2, 22.5, 13.9. Spectral data were consistent with those previously reported.[121]

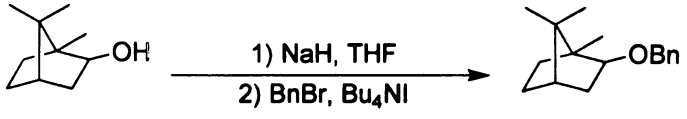


Preparation of 4'-acetoxyacetophenone: a 50 mL round bottom flask was charged with 1.0 equiv 4'-hydroxyacetophenone (20 mmol, 2.72 g) and excess acetic anhydride (10 mL). The mixture was stirred vigorously and excess dry pyridine (10 mL) was added slowly. The reaction was stirred overnight, then poured into an erylmer with ice and 1 M HCl, followed by extraction with ether. The ether extract was washed with water, dried over $MgSO_4$, and concentrated, affording a liquid which crystallized upon sitting overnight. The clear crystalline solid was rinsed with water to afford 2.23 g (62%). ^1H NMR (300 MHz, $CDCl_3$), δ 7.96 (d, J = 8.24 Hz, 2H), 7.16 (d, J = 8.79 Hz, 2H), 2.56 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 196.7, 168.8, 154.2, 134.6, 129.8, 121.7, 26.5, 21.1. Spectral data were consistent with those previously reported.[122]



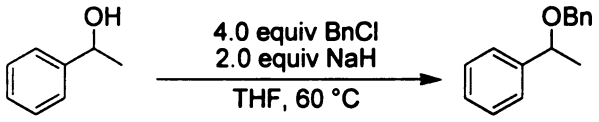
Preparation of 4-(4-acetyl-phenyl)-butane-2-one:[123] a 25 mL round bottom was charged with 1.0 equiv 4'-iodoacetophenone (20 mmol, 4.92 g), 3 mol% $Pd(OAc)_2$ (0.6 mmol, 0.135 g), and 10 mL CH_3CN. The r.b. was connected to a reflux condenser and flushed with nitrogen, then 1.25 equiv 3-butene-2-ol (25 mmol, 2.17 mL) and 1.25 equiv Et_3N (25 mmol, 3.48 mL) were injected into the

reaction. The r.b. was placed in an oil bath at 100 °C and the reaction was refluxed for 16 hours. The reaction mixture was cooled to room temperature and diluted with water and ether. The two layers were separated and the ether layer was washed with water. The aqueous layer was back extracted with ether. The combined organics were dried over $MgSO_4$, and concentrated. The crude reddish-orange material was subjected to column chromatography with hexanes / ethyl acetate (95/5 then 80/20) affording 2.86 g (75%) of yellow solid. ^1H NMR (300 MHz, $CDCl_3$), δ 7.85 (d, *J* = 8.24 Hz, 2H), 7.25 (d, *J* = 8.24 Hz, 2H), 2.91 (m, 2H), 2.77 (m, 2H), 2.54 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 207.20, 197.70, 146.75, 135.19, 128.57, 128.49, 44.14, 30.01, 29.47, 26.51. Spectral data were consistent with those previously reported.[124]



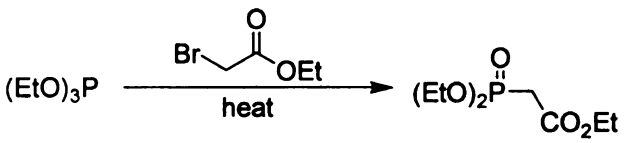
Benzyl-bornyl ether[125] was prepared by charging a three-necked round bottom, equipped with a reflux condenser and addition funnel, with 1.0 equiv DL-isoborneol (30.0 mmol, 4.63 g) and 150 mL THF. The r.b. was place under a nitrogen atmosphere and 2.0 equiv NaH (60 mmol, 2.4g, 60% mineral dispersion) was added in four portions, with 5 minutes of stirring between each portion. The mixture was then heated to reflux for 30 minutes, then cooled to room temperature, at which point 2.0 equiv benzyl bromide (60.0 mmol, 7.14 mL, filtered through neutral aluminum oxide) was injected into the addition funnel with 50 mL THF, which was added drop wise to the reaction over 30 minutes; followed by 0.1 equiv tetrabutylammonium iodide (3.0 mmol, 1.1 g) in 5 mL DMF

being added in one portion. The reaction was stirred over night, then reheated to reflux for 1 hour. The reaction was cooled, quenched with water, and extracted with ether. The organic layer was dried over $MgSO_4$, concentrated, and subjected to column chromatography with hexanes / ethyl acetate (100/0, 99/1, 95/5, 90/10, 80/20) affording 7.185 g (98%) of a clear oil. ^1H NMR (300 MHz, $CDCl_3$), δ 7.35 – 7.18 (m, 5H), 4.57 (d, *J* = 12.086 Hz, 1H), 4.40 (d, *J* = 12.636 Hz, 1H), 3.33 (dd, *J* = 1.69, 7.14 Hz, 1H), 1.91 – 1.81 (m, 1H), 1.76 – 1.45 (m, 4H), 1.07 (s, 3H), 1.01 (s, 1H), 0.98 (s, 4H), 0.85 (s, 3H): ^{13}C NMR (75 MHz, $CDCl_3$), δ 139.6, 128.1, 126.9, 86.5, 70.5, 49.3, 46.5, 45.1, 38.4, 34.4, 27.3, 20.3, 20.2, 11.9.

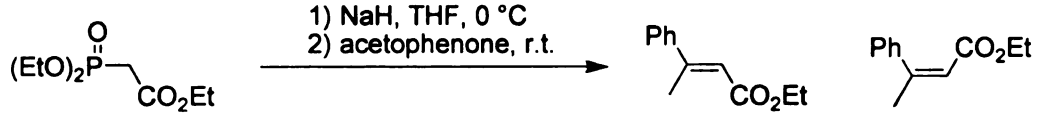


Benzyl-(1-phenylethyl)-ether was prepared by charging a 250 mL round bottom flask equipped with a reflux condesor, with 2.0 equiv NaH (33.2 mmol, 0.797 g), in a 60% mineral dispersion (weighed out 1.328 g); which was triple washed with hexanes and dried under high vacuum. The sodium hydride was suspended in 30 mL of THF under nitrogen. The mixture was stirred vigorously and a solution of 1 equiv *sec*-phenethyl alcohol (16.6 mmol, 2.0 mL) in 70 mL THF was added slowly over 15 minutes. The mixture was stirred for 30 minutes at room temperature, the r.b. was then placed in an oil bath at 60 °C, followed by the addition of 4.0 equiv benzyl chloride (66.4 mmol, 7.6 mL). The reaction was stirred overnight (10 hours). The reaction was quenched with sat. NH_4Cl (aq), diluted with water, and extracted with ether. The ether extracts were washed

with water and brine, dried over $MgSO_4$, and concentrated. The crude material was subjected to column chromatography with hexanes / ethyl acetate (100/0, 90/10, 70/30, then 50/50) affording 2.48 g (70%) of light yellow liquid. ^1H NMR (300 MHz, $CDCl_3$), δ 7.46 – 7.33 (m, 10H), 4.59 (q, *J* = 6.59 Hz, 1H), 4.48 (dd, *J* = 12.08, 35.70 Hz, 2H), 1.58 (d, *J* = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 143.6, 138.5, 128.4, 128.3, 127.6, 127.4, 127.4, 126.3, 77.1, 70.2, 24.2. Spectral data were consistent with those previously reported.[126]



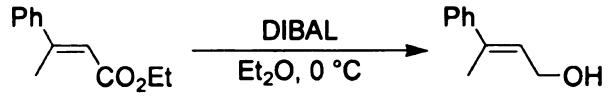
Triethyl phosphonoacetate[127] was prepared by placing freshly distilled triethyl phospite (204 mmol, 34.98 mL) in a 100 mL three-necked round bottom equipped with a dropping funnel, stir bar, and short path distillation head. The addition funnel was charged with ethyl bromoacetate (200 mmol, 22.18 mL) which was added drop wise to the r.b. over an hour. The r.b. was then placed in an oil bath at 85 °C (heated to 100 °C) to distill of the ethyl bromide formed. After removal of most of the EtBr, the oil bath was heated to 170 °C for 7 hours. The crude material was cooled then subjected to distillation under reduced pressure with a high vacuum (distilled at 98 °C, 1mm Hg, oil bath 110 °C) affording 41.15 g (86%) of a clear liquid. ^1H NMR (300 MHz, $CDCl_3$), δ 4.23 – 4.02 (m, 6H), 2.94 (s, 1H), 2.87 (s, 1H), 1.36 – 1.16 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 165.8, 62.5, 61.5, 35.2, 16.2, 14.0. Spectral data were consistent with commercially available material.



E/Z = 5.4/1 crude
= 5.783/1 isolated

Procedure for the preparation of (E/Z) 3-phenyl-but-2-enoic acid ethyl ester:[128] a 100 ml three-necked round bottom was charged with 1.5 equiv NaH (46.87 mmol, 1.86 g, 60% mineral dispersion), which was triple washed with hexanes under a blanket of nitrogen, then dried under vacuum. The dry NaH was dissolved in 40 mL THF, and a reflux condenser and addition funnel were attached to the r.b., with a positive flow of nitrogen. The r.b. was placed in an ice bath followed by the drop wise addition of 1.6 equiv triethyl phosphonoacetate (50 mmol, 10.54 mL) over 30 minutes. The r.b. was warmed to r.t. and 1.0 equiv acetophenone (31.25 mmol, 3.64 mL), in 20 mL THF, was added drop wise over 30 minutes, and the reaction was stirred overnight. The reaction mixture was poured into a sep. funnel with water (30 mL) and ether (70 mL). The ether layer was washed with brine and the combined aqueous layers were back extracted with ether. The combined organics were dried over $MgSO_4$, and concentrated, affording a light yellow oil (E/Z = 5.4/1). The crude material was subjected to column chromatography with hexanes / ethyl acetate (99/1, 95/5, 90/10) affording 5.892 g (99%) of pure product, of which 5.023 g (84.5%) was the E alkene (light yellow oil) and 0.869 g (14.6%) was the Z alkene (light yellow oil) (E/Z = 5.78/1). (E-olefin) ^1H NMR (300 MHz, $CDCl_3$), δ 7.44 (m, 2H), 7.33 (m, 3H), 6.12 (s, 1H), 4.19 (q, J = 7.14 Hz, 2H), 2.56 (s, 3H), 1.29 (t, J = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 166.8, 155.4, 142.1, 128.9, 128.4, 126.2, 117.0, 59.7, 17.8, 14.2;

(Z-olefin) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.3 (m, 3H), 7.18 (d, *J* = 6.04, 2H), 5.89 (s, 1H), 3.97 (q, *J* = 7.14 Hz, 2H), 2.15 (s, 3H), 1.06 (t, *J* = 7.14 Hz, 3H). Spectral data were consistent with those previously reported.[129]

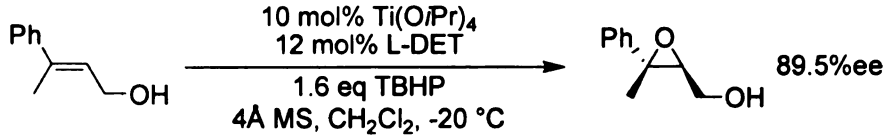


Procedure for the preparation of (E)-3-phenyl-2-buten-1-ol:[130] a 250 mL three-necked round bottom was connected to a reflux condenser, sealed, and placed under a positive flow of nitrogen. The r.b. was charged with 1.0 equiv (E)-3-phenyl-but-2-enoic acid ethyl ester (21 mmol, 4.0 g) and 48 mL of anhydrous ether, then place in an ice bath. When the ethereal solution reached 0 °C, 2.2 equiv DIBAL (46.25 mmol, 1 M solution in hexanes, 46.25 mL) was added slowly over 20 minutes from a syringe. The reaction was stirred to r.t. then stirred over night (10 hours). The r.b. was placed in an ice bath, then the reaction was quenched by slow addition of water, then brine. The white solid material formed was dissolved by the addition of 4 M HCl till there was two clear layers. The aqueous layer was back extracted with ether, and the combined organics were dried over $MgSO_4$, and concentrated. The crude material was subjected to column chromatography with hexanes / ethyl acetate (80/20 then 50/50) affording 3.033 g (97%) of light yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.42 – 7.36 (m, 2H), 7.34 – 7.20 (m, 3H), 5.96 (t, *J* = 6.59 Hz, 1H), 4.33 (d, *J* = 6.04 Hz, 2H), 2.05 (s, 3H), 1.75 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 142.7, 137.6, 128.2, 127.2, 126.4, 125.7, 59.8, 15.9. Spectral data were consistent with those previously reported.

Procedure for the preparation of (Z)-3-phenyl-2-buten-1-ol: a 250 mL three-necked round bottom was connected to a reflux condenser, sealed, and placed under a positive flow of nitrogen. The r.b. was charged with 1.0 eq. (Z)-3-phenyl-but-2-enoic acid ethyl ester (30 mmol, 5.707g) and 68 mL of anhydrous ether, then place in an ice bath. When the ethereal solution reached 0°C, 2.2 eq. DIBAL (66 mmol, 1 M solution in hexanes, 66 mL) was added slowly over 20 minutes from a syringe. The reaction was stirred to r.t. then stirred over night (10 hours). The r.b. was placed in an ice bath, then the reaction was quenched by slow addition of water, then brine. The white solid material formed was dissolved by the addition of 4 M HCl till there was two clear layers. The aqueous layer was back extracted with ether, and the combined organics were dried over $MgSO_4$, and concentrated. The crude material was subjected to column chromatography with hexanes / ethyl acetate (80/20 then 50/50) affording 4.2g (94.46%) of light yellow liquid. ^1H NMR (300 MHz, $CDCl_3$), δ 7.36 – 7.21 (m, 3H), 7.20 – 7.12 (m, 2H), 5.67 (t, J = 6.86 Hz, 1H), 4.02 (d, J = 7.14 Hz, 2H), 2.61 (bs, 1H: OH), 2.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 140.64, 139.39, 127.93, 127.60, 126.93, 126.16, 59.80, 25.09. Spectral data were consistent with those previously reported.

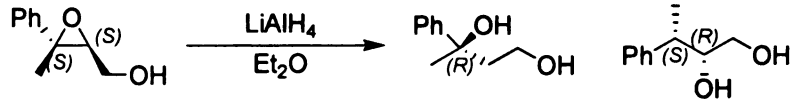
Procedure for the preparation of anhydrous *tert*-butylhydrogen peroxide (TBHP): to a 1 L sep. funnel was added 360 mL of *tert*-butylhydrogen peroxide (30% aqueous solution) and 440 mL of toluene. The solution was swirled for 1 minute (not shaken!). The aqueous phase was separated and the organic layer

was transferred to a 1 L round bottom equipped with a Dean-Stark trap and reflux condenser. Boiling chips were added and the solution was refluxed for 4 hours. The TBHP-toluene solution was cooled then transferred to an amber glass bottle with activated 4Å MS. The bottle was sealed and place under nitrogen, and stored in the freezer. The molarity of the solution was determined by NMR and found to be 3.9 M.



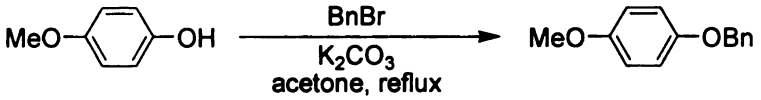
Procedure for the preparation of 2,3-epoxy-3-phenylbutan-1-ol via a Sharpless asymmetric epoxidation: a 250 mL three-necked round bottom, equipped with a thermoter and stir-bar, was charged with activated 4Å MS (3.6 g) and freshly distilled CH_2Cl_2 (130 mL) under nitrogen. The CH_2Cl_2 solution was cooled to –22 °C, followed by sequential addition of 0.12 equiv L-diethyl tartrate (2.45 mmol, 0.421 mL), 0.1 equiv titanium isopropoxide (2.04 mmol, 0.609 mL), and drop wise addition of 1.6 equiv TBHP (32.74 mmol, 8.4 mL, 3.9M solution in toluene). The mixture was stirred for 1 hour at –22 °C, followed by the drop wise addition of 1.0 equiv (E)-3-phenyl-2-butene-1-ol (20.46 mmol, 3.03 g) in 6 mL CH_2Cl_2, making sure the temperature did not go above -20°C. After complete addition the reaction was stirred at -25°C for 6 hours. The reaction was quenched with 15 mL of a 10% NaOH solution saturated with NaCl. The reaction was warmed to -10°C and $MgSO_4$ (8 g), Celite (2 g), and ether were added. The reaction was warmed to room temperature and filtered through a pad of celite. The filtrate was concentrated and the crude material was subjected

to flash chromatography with hexanes / ethyl acetate affording 2.309 g of epoxide as a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.37 (m, 5H), 3.92 (m, 1H), 3.80 (m, 1H), 3.07 (dd, *J* = 2.19, 6.04 Hz, 1H), 2.68 (bs, 1H), 1.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 141.8, 128.2, 127.4, 124.9, 66.1, 61.1, 60.8, 17.6. %ee determined by GC using a Beta DEX™ 325 Fused Silica Capilary Column: 30mX0.25mmX0.25μm film thickness. GC conditions: starting temperature (30 °C), ramp rate (10 °C/min.), final temperature (200 °C for 15 min.), R.T. 13.96 (5.3%: 2R,3R-enantiomer), 19.75 (94.7%: 2S,3S-enantiomer), 89.47% ee. Spectral data were consistent with those previously reported.[130]



Procedure for the preparation of (R)-3-phenyl-butane-1,3-diol and (2R,3S)-3-phenyl-butane-1,2-diol:[131] a 100 mL round bottom equipped a stir bar and reflux condenser was charged with 2.0 equiv $LiAlH_4$ (7.8 mmol, 0.296 g). The round bottom was placed under an atmosphere of nitrogen and 35 mL of anhydrous ether was added. To the stirred solution of LAH, 1.0 equiv of 2S,3S-epoxy-3-phenyl-butan-1-ol (3.9 mmol, 0.640 g) in 10 mL of anhydrous ether was added drop wise, followed by stirring the reaction for 3 hours. The reaction was quenched with 2 mL of H_2O, 0.5 mL 1 M NaOH, and 6 mL H_2O (all added drop wise until vigorous bubbling stopped). The solid white material was filtered off and rinsed with ether. The ethereal solution was dried over $MgSO_4$, filtered, and concentrated. NMR of the crude material showed a mixture of the 1,3 and 1,2-diol (1.07/1). The crude material was subjected to FC with hexanes / ethyl

acetate (90/10, 80/20, 50/50, then 20/80) affording 0.5407 g of material: 0.2528 g (39%) of (R)-3-phenyl-butane-1,3-diol as a white solid; mp = 62-63.5 °C; and 0.2879 g (44%) of (2R,3S)-3-phenyl-butane-1,2-diol as a clear viscous oil. 1,3-diol; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.42 (d, *J* = 7.14 Hz, 2H), 7.33 (t, *J* = 7.69 Hz, 2H), 7.23 (t, *J* = 3.57 Hz, 1H), 3.74 (bs, 1H), 3.54 (t, *J* = 8.79 Hz, 1H), 3.46 (d, *J* = 5.49, 1H), 2.37 (bs, 1H), 2.03 (m, 2H), 1.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 147.4, 128.2, 126.5, 124.7, 75.8, 60.3, 43.9, 31.0. 1,2-diol; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.31 – 7.11 (m, 5H), 3.68 (t, *J* = 6.59 Hz, 1H), 3.37 (bs, 2H), 3.27 (m, 1H), 3.15 (bs, 1H), 2.72 (q, *J* = 7.42 Hz, 1H), 1.31 (d, *J* = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 143.7, 128.5, 127.4, 126.5, 76.5, 65.0, 42.8, 17.5. The %ee of the 1,3-diol was determined by derivatization with Mosher's acid chloride: a flame dried 5mL test tube was charged with 1.0 equiv 3-phenyl-butan-1,3-diol (0.1413 mmol, 0.023 g), a crystal of DMAP, and a stir bar. The test tube was sealed with a septa, rapped with Teflon tap, and flushed with nitrogen. Dry CH_2Cl_2 (1 mL), 4 drops of Et_3N (freshly distilled), and 1.4 equiv (S)-(+)-MTPA-Cl (0.1979 mmol, 0.05 g) were injected sequentially, and the reaction was stirred over night. The reaction mixture was subjected to FC with hexanes / ethyl acetate (80/20, then 50/50) affording the ester. ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.49 – 7.18 (m, 10H), 4.24 (t, *J* = 8.24 Hz, 2H), 3.49 (s, 3H), 2.20 (t, *J* = 6.87 Hz, 2H), 1.61 (s, 0.27H), 1.53 (s, 2.77H): (S,R) vs (R,R) = 1 / 10.65: de = 82.84%; ^{13}C NMR (75 MHz, $CDCl_3$), δ 166.3, 146.3, 132.0, 129.6, 128.4, 128.4, 127.1, 126.9, 124.4, 73.6, 63.6, 55.4, 41.5, 30.7.

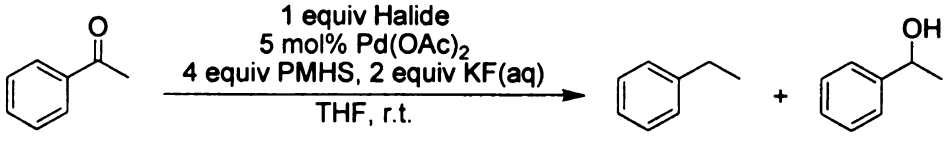


Procedure for the preparation of 1-benzyloxy-4-methoxy-benzene: An oven dried 50 mL round bottom was charged with 1.0 equiv 4-methoxyphenol (20 mmol, 2.483 g), 1.3 equiv potassium carbonate (26 mmol, 3.593 g), and dry acetone. The R.B. was connected to a reflux condenser and flushed with nitrogen. A balloon of nitrogen was attached to the system, followed by placing the R.B. in an oil-bath at 70 °C and stirring the reaction. The reaction was heated for ~10 minutes followed by the slow addition of 1.3 equiv benzyl bromide (26 mmol, 3.09 mL). The reaction was refluxed for 18 hours, cooled to room temperature, and diluted with water and ether. The organic layer was sequentially washed with 10% H_2SO_4 and 1M NaOH, dried over $MgSO_4$, and concentrated. The crude material was subjected to FC with hexanes / ethyl acetate (99/1, 98/2, 95/5, then 90/10) affording 3.752 g (87%) of white fluffy powder; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.37 (m, 5H), 6.89 (d, J = 9.34 Hz, 2H), 6.81 (d, J = 9.34 Hz, 2H), 4.99 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 153.9, 152.9, 137.2, 128.5, 127.8, 127.4, 115.8, 114.6, 70.6, 55.6. Spectral data were consistent with those previously reported.[132]

General Procedure C

General Procedure for the Reductive Bond Cleavage of Benzylic C-O Bonds: A 25 mL round bottom was charged with $Pd(OAc)_2$ (0.05 mmol, 0.011 g), ketone (1.0 mmol), and freshly distilled THF (5 mL). The round bottom was sealed with a septa and flushed with nitrogen. Potassium fluoride (4 mmol, 0.232 g) was taken up with degassed water (2 mL) and injected into the reaction flask, followed by attacking a balloon of nitrogen, then injecting chlorobenzene (0.1 mmol, 0.01 mL) or 4-chloroanisole (0.1 mmol, 0.011 mL). PMHS (2.5 mmol, 0.15 mL) was injected into the reaction mixture dropwise, and the reaction was stirred for one hour (***Caution**: Rapid addition PMHS can result in uncontrollable gas evolution!*). Ether was added to the reaction mixture, the layers were separated, and the aqueous layer was back extracted with ether. The combined organics were concentrated and subjected to flash chromatography. (**Caution**: Reaction is exothermic upon addition of PMHS, so when running on large scale the use of a reflux condenser is recommended.)

*To ensure complete removal of silane byproduct, the combined organics may also be filtered through a plug of Celite (top layer) and neutral alumina (bottom layer) in a 1 cm diameter column by flushing with EtOAc, concentrated, then subjected to silica gel FC.



Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of chlorobenzene (1 mmol, 0.101 mL),

acetophenone (1 mmol, 0.117 mL) was reduced affording 100% ethyl benzene as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of bromobenzene (1 mmol, 0.105 mL), acetophenone (1 mmol, 0.117 mL) was reduced affording 22% ethyl benzene and 78% *sec*-phenethyl alcohol as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of iodobenzene (1 mmol, 0.112 mL), acetophenone (1 mmol, 0.117 mL) was reduced affording 25% *sec*-phenethyl alcohol as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of tetrabutylammonium chloride (1 mmol, 0.278 g), acetophenone (1 mmol, 0.117 mL) was reduced affording 30% *sec*-phenethyl alcohol as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL). The reaction mixture polymerized at 3.5 hours.

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of cesium chloride (1 mmol, 0.168 g), acetophenone (1 mmol, 0.117 mL) was reduced affording 98% *sec*-phenethyl

alcohol as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of lithium chloride (1 mmol, 0.042 g), acetophenone (1 mmol, 0.117 mL) was reduced affording 99% *sec*-phenethyl alcohol as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of phenyl nonaflate (1 mmol, 0.360 g), acetophenone (1 mmol, 0.117 mL) was reduced affording 99% *sec*-phenethyl alcohol as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), 1 equiv of phenyl nonaflate (1 mmol, 0.360 g), and 1 equiv lithium chloride (1 mmol, 0.042 g), acetophenone (1 mmol, 0.117 mL) was reduced affording 97% ethylbenzene as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of benzyl chloride (1 mmol, 0.115 mL), acetophenone (1 mmol, 0.117 mL) was reduced affording 100% ethyl benzene as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of 1-chlorobutane (1 mmol, 0.104 mL), acetophenone (1 mmol, 0.117 mL) was reduced affording 25% *sec*-phenethyl alcohol as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of hydrochloric acid (1 mmol, 11.6 M solution, 0.086 mL), acetophenone (1 mmol, 0.117 mL) was reduced affording 22% ethyl benzene and 78% *sec*-phenethyl alcohol as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 2 equiv of KF (2 mmol, 0.116 g), and 1 equiv of chlorotrimethylsilane (1 mmol, 0.127 mL), acetophenone (1 mmol, 0.117 mL) was reduced affording 95% ethyl benzene as determined by ^{1}H NMR with an internal standard (CH_2Cl_2, 1 mmol, 0.064 mL).

Following general procedure C with chlorobenzene (0.1 mmol, 0.01 mL), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.035 g (21%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1418 g (79%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 2-chloro-*m*-xylene (0.1 mmol, 0.013 mL), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0217 g (13%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1331 g (74%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 4-chloroanisole (0.1 mmol, 0.012 mL), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0634 g (37%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.083 g (46%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 4-chlorobenzotrifluoride (0.1 mmol, 0.01s mL), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0553 g (32%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.0513 g (28%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 2-chloropyridine (0.1 mmol, 0.009 mL), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0234 g (13%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil, and 0.1526 g (85%) of starting material.

Following general procedure C with ortho-dichlorobenzene (0.1 mmol, 0.011 mL), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0623 g (38%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1100 g (61%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with hexachlorobenzene (0.1 mmol, 0.028 g), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0477 g (29%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1313 g (67%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 4-chloroanisole (0.1 mmol, 0.012 mL) and 0.1 equiv of 2,6-lutidine (0.1 mmol, 0.011 mL), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.1701 g (94%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

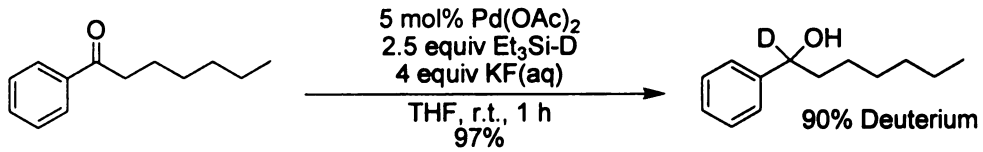
Following general procedure C with 4-chloroanisole (0.1 mmol, 0.012 mL) and 0.1 equiv of 2,6-di-*tert*-butyl-4-methylpyridine (0.1 mmol, 0.02 g), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0553 g (34%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1119 g (62%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 4-chloroanisole (0.1 mmol, 0.012 mL) and 0.5 equiv of 2,6-di-*tert*-butyl-4-methylpyridine (0.5 mmol, 0.102 g), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0373 g (23%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1171 g (65%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 4-chloroanisole (0.1 mmol, 0.012 mL) and 0.5 equiv of Proton-Sponge® (0.5 mmol, 0.107 g), methyl 4-acetyl benzoate (1

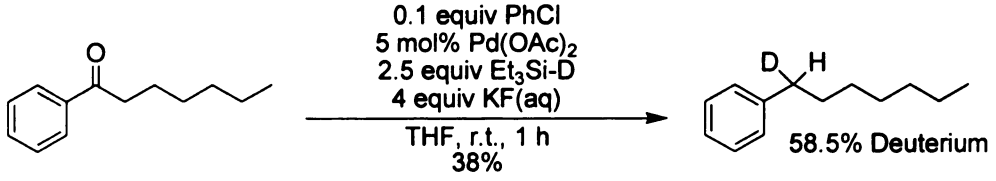
mmol, 0.178 g) was reduced affording 0.1607 g (98%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 4-chloroanisole (0.1 mmol, 0.012 mL) and 0.5 equiv of propylene oxide (0.5 mmol, 0.035 mL), methyl 4-acetyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0613 g (37%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1035 g (57%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

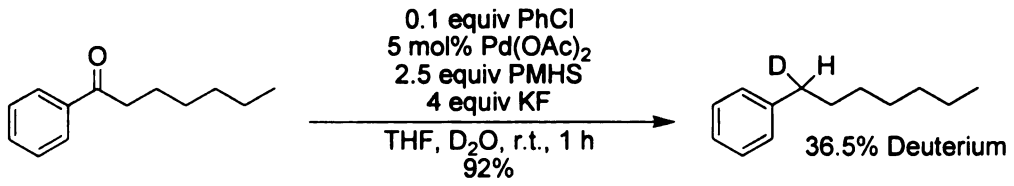


A dry 25 mL r.b. was charged with $Pd(OAc)_2$ (0.085 mmol, 0.019 g), KF (6.8 mmol, 0.395 g), sealed, and flushed with nitrogen. While flushing the system, 8.5 mL of freshly distilled THF, 1-phenyl-octan-1-one (1 mmol, 0.368 mL), and 3.4 mL of degassed water were injected sequentially. The nitrogen line was removed and a balloon of nitrogen was attached. Trethylsilane-d (4.26 mmol, 0.5 g, 97% deuterium) was slowly injected dropwise followed by stirring for 1 hour. The reaction was diluted with ether, the layers separated, and the aqueous layer back extracted with ether. The combined organics were filtered through a plug of Celite (top layer) and neutral alumina (bottom layer) with EtOAc. The filtrate was concentrated then subjected to flash chromatography (hexanes/EtOAc: 100/0 then 95/5) affording 0.7871 g of 1-phenyloctan-1-ol (97%) and triethylsilanol as a clear oil. %Deuterium incorporation was determined by ^1H NMR; ^1H NMR (300

MHz, $CDCl_3$), δ 7.30 (m, 5H), 4.61 (t, *J* = 6.59 Hz, 1H, measured 0.1H, 90% deuterium), 2.09 (bs, 1H), 1.85-1.59 (m, 2H), 1.22 (m, 10H), 0.83 (m, 3H).



A dry 25 mL r.b. was charged with $Pd(OAc)_2$ (0.08 mmol, 0.017 g), KF (6.8 mmol, 0.395 g), sealed, and flushed with nitrogen. While flushing the system, 8.5 mL of freshly distilled THF, 1-phenyl-octan-1-one (1.7 mmol, 0.368 mL), chlorobenzene (0.17 mmol, 0.017 mL), and 3.4 mL of degassed water were injected sequentially. The nitrogen line was removed and a balloon of nitrogen was attached. Trethylsilane-d (4.26 mmol, 0.5 g, 97% deuterium) was slowly injected dropwise followed by stirring for 1 hour. The reaction was diluted with ether, the layers separated, and the aqueous layer back extracted with ether. The combined organics were filtered through a plug of Celite (top layer) and neutral alumina (bottom layer) with EtOAc. The filtrate was concentrated then subjected to flash chromatography (hexanes/EtOAc: 100/0 then 95/5) affording 0.122 g (38%) of 1-phenyloctane as a clear oil. %Deuterium incorporation was determined by ^1H NMR; ^1H NMR (300 MHz, $CDCl_3$), δ 7.26 (m, 5 H), 2.64 (m, 2H, measured 0.85 H, 57.5% deuterium), 1.64 (m, 2H), 1.32 (m, 10 H), 0.93 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 142.8, 128.3, 128.1, 125.5, 36.0, 35.8, 35.6, 35.3, 31.9, 31.5, 31.48, 31.40, 29.5, 29.3, 29.2, 22.6, 14.1.

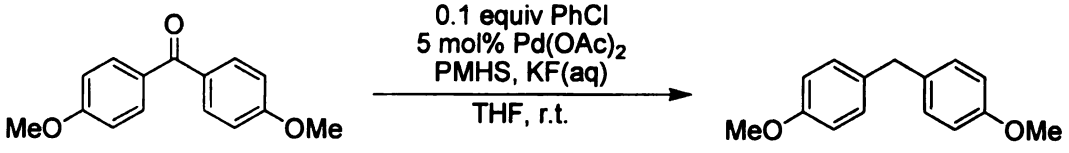


A dry 25 mL r.b. was charged with $Pd(OAc)_2$ (0.05 mmol, 0.011 g), KF (4 mmol, 0.232 g), sealed, and flushed with nitrogen. While flushing the system, 5 mL of freshly distilled THF, 1-phenyl-octan-1-one (1 mmol, 0.216 mL), chlorobenzene (0.1 mmol, 0.01 mL), and 2 mL of deuterium oxide (D_2O) were injected sequentially. The nitrogen line was removed and a balloon of nitrogen was attached. PMHS (2.5 mmol, 0.15 mL) was slowly injected dropwise followed by stirring for 1 hour. The reaction was diluted with ether, the layers separated, and the aqueous layer back extracted with ether. The combined organics were filtered through a plug of Celite (top layer) and neutral alumina (bottom layer) with EtOAc. The filtrate was concentrated then subjected to flash chromatography (hexanes/EtOAc: 100/0 then 95/5) affording 0.1752 g (92%) of 1-phenyloctane as a clear oil. %Deuterium incorporation was determined by ^1H NMR; ^1H NMR (300 MHz, $CDCl_3$), δ 7.26 (m, 5H), 2.64 (m, 2H, measured 1.27H, 36.5% deuterium), 1.65 (m, 2H), 1.32 (m, 10H), 0.93 (m, 3H); 142.9, 128.3, 128.1, 125.5, 36.0, 31.9, 31.5, 31.4, 29.5, 29.37, 29.34, 29.2, 22.6, 14.1.

Following general procedure C 1-phenyl-octan-1-one (1 mmol, 0.217 mL) was reduced, affording 0.1759 g (92%) of octyl-benzene as a clear liquid (silica gel FC, hexanes); ^1H NMR (300 MHz, $CDCl_3$), δ 7.20 (m, 2H), 7.11 (m, 3H), 2.54 (t, *J*

= 7.69 Hz, 2H), 1.55 (m, 2H), 1.21 (m, 10H), 0.82 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 142.9, 128.3, 128.1, 125.5, 36.0, 31.9, 31.5, 29.5, 29.3, 29.2, 22.6, 14. Physical and spectral data were consistent with commercially available material.

Following general procedure C in the absence of an aromatic chloride, with 1.5 equiv of PMHS (1.5 mmol, 0.09 mL) and 2 equiv KF (2 mmol, 0.116 g), 1-phenyl-octan-1-one (1 mmol, 0.217 mL) was reduced affording 0.182 g (88%) of 1-phenyl-octan-1-ol as a clear liquid (silica gel FC, hexanes/EtOAc: 95/5); ^1H NMR (300 MHz, $CDCl_3$), δ 7.31 (m, 5H), 4.59 (t, J = 6.59 Hz, 1H), 2.33 (s, 1H), 1.83 – 1.58 (m, 2H), 1.26 (m, 10H), 0.87 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 144.9, 128.2, 127.0, 125.8, 74.5, 39.0, 31.7, 29.4, 29.1, 25.7, 22.5, 14.0. Physical and spectral data were consistent with commercially available material.



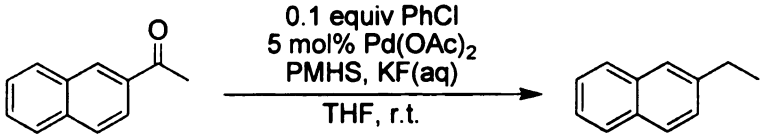
Following general procedure C 4,4'-dimethoxy-benzophenone (1 mmol, 0.242 g) was reduced, affording 0.2166 g (95%) of bis-(4-methoxy phenyl)-methane as a white solid (silica gel FC, hexanes/EtOAc: 95/5); mp = 52 °C; ^1H NMR (300 MHz, $CDCl_3$), δ 7.14 (d, J = 8.14 Hz, 4H), 6.88 (d, J = 8.14 Hz, 4H), 3.92 (s, 2H), 3.81 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 157.7, 133.6, 129.6, 113.7, 55.0, 40.0. Physical and spectral data were consistent with literature. [133]

Following general procedure C benzoylcylobutane (1 mmol, 0.152 mL) was reduced, affording 0.1059 g (72%) of benzylcyclobutane as a clear oil, and 0.0337 g (21%) of 1-cyclobutyl-1-phenylmethanol as light yellow oil (silica gel FC, hexanes/EtOAc: 95/5 then 80/20); (benzylcyclobutane) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.31 (t, J = 7.14 Hz, 2H), 7.19 (m, 3H), 2.74 (d, J = 7.69, 2H), 2.62 (sep, J = 7.69, 1H), 2.09 (m, 2H), 1.96 – 1.69 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 141.2, 128.4, 128.1, 125.5, 42.9, 37.2, 28.2, 18.3; spectral data was consistent with literature[134]; (1-cyclobutyl-1-phenylmethanol) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.16 (m, 5H), 4.38 (d, J = 8.24 Hz, 1H), 2.48 (m, 1H), 2.18 (s, 1H), 1.88 (m, 2H), 1.65 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 143.0, 128.1, 127.3, 126.0, 78.2, 42.2, 24.7, 24.2, 17.6; spectral data were consistent with literature.[135]

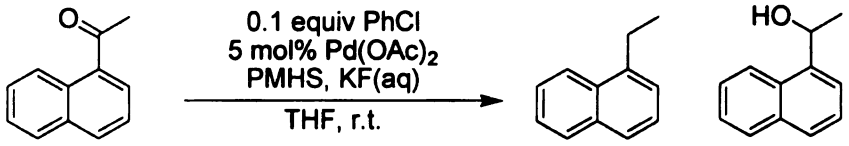
Following general procedure C with 4 equiv PMHS (4 mmol, 0.24 mL) benzoylcylobutane (1 mmol, 0.152 mL) was reduced, affording 0.1209 g (83%) of benzylcyclobutane as a clear oil, and 0.0201 g (12%) of 1-cyclobutyl-1-phenylmethanol.

Following general procedure C with 4 equiv PMHS (4 mmol, 0.24 mL), and 0.1 equiv 4-chloroanisole (0.1 mmol, 0.012 mL), benzoylcylobutane (1 mmol, 0.152 mL) was reduced, affording 0.1374 g (94%) of benzylcyclobutane as a clear oil.

Following general procedure C in the absence of an aromatic chloride, with 1.5 equiv of PMHS (1.5 mmol, 0.09 mL) and 2 equiv KF (2 mmol, 0.116 g), benzoylcylobutane (1 mmol, 0.152 mL) was reduced affording 0.1621 g (99%) of 1-cyclobutyl-1-phenylmethanol.



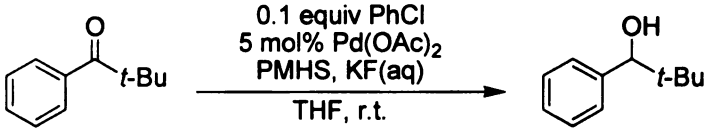
Following general procedure C 2-acetylnaphthalene (1 mmol, 0.170 g) was reduced, affording 0.1306 g (84%) of 2-ethylnaphthalene as a light yellow liquid (silica gel FC, hexanes/EtOAc: 95/5); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.87 (m, 3H), 7.72 (s, 1H), 7.57 – 7.40 (m, 3H), 2.9 (q, *J* = 7.69 Hz, 2H), 1.42 (t, *J* = 7.69 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 141.6, 133.6, 131.9, 127.7, 127.5, 127.3, 127.0, 125.7, 125.5, 124.9, 29.0, 15.5. Physical and spectral data were consistent with commercially available material.



Following general procedure C 1-acetylnaphthalene (1 mmol, 0.152 mL) was reduced, affording 0.1249 g (80%) of 1-ethylnaphthalene as a light yellow liquid, and 0.0327 g (19%) of 1-[1]naphthyl-ethanol as a clear oil (silica gel FC, hexanes/EtOAc: 95/5 then 80/20); (1-ethylnaphthalene) ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.07 (d, *J* = 8.24 Hz, 1H), 7.86 (d, *J* = 9.34 Hz, 1H), 7.72 (d, *J* = 8.24 Hz, 1H), 7.56 – 7.32 (m, 4H), 3.13 (q, *J* = 7.69 Hz, 2H), 1.39 (t, *J* = 7.69, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 140.2, 133.8, 131.8, 128.7, 126.3, 125.6, 125.3, 124.8, 123.6, 23.8, 14.9; Physical and spectral data were consistent with commercially available material. (1-[1]naphthyl-ethanol) ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.06 (m, 1H), 7.86 (m, 1H), 7.75 (d, *J* = 8.24 Hz, 1H), 7.64 (d, *J* = 7.14 Hz, 1H), 7.49 (m, 3H), 5.58 (q, *J* = 6.59 Hz, 1H), 2.62 (bs, 1H), 1.61 (d, *J* = 6.59 Hz, 3H); ^{13}C NMR

(75 MHz, $CDCl_3$), δ 141.2, 133.6, 130.1, 128.7, 127.7, 125.8, 125.4, 123.0, 121.9, 66.8, 24.2. Physical and spectral data were consistent with commercially available material.

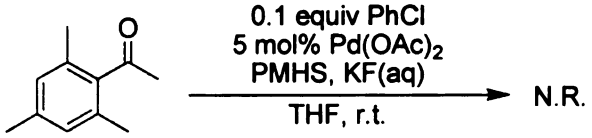
Following general procedure C with 0.1 equiv of 4-chloroanisole (0.1 mmol, 0.012 mL) 1-acetylnaphthalene (1 mmol, 0.152 mL) was reduced affording 0.1546 g (99%) of 1-ethylnaphthalene.



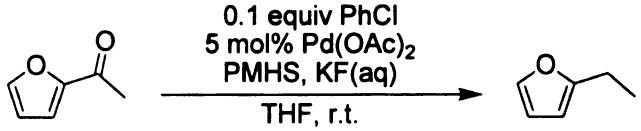
Following general procedure C 2,2-dimethyl-1-phenyl-propan-1-one (1 mmol, 0.167 mL) was reduced, affording 0.1573 g (96%) of 2,2-dimethyl-1-phenyl-propan-1-ol as a white solid (silica gel FC, hexanes/EtOAc: 95/5); mp = 44 °C; ^1H NMR (300 MHz, $CDCl_3$), δ 7.24 (s, 5H), 4.30 (s, 1H), 2.08 (s, 1H), 0.87 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 142.1, 127.5, 127.4, 127.1, 82.2, 35.4, 25.8. Physical and spectral data were consistent with commercially available material.

Following general procedure C with 4 equiv PMHS (4 mmol, 0.24 mL) 2,2-dimethyl-1-phenyl-propan-1-one (1 mmol, 0.167 mL) was reduced, affording 0.164 g (100%) of 2,2-dimethyl-1-phenyl-propan-1-ol.

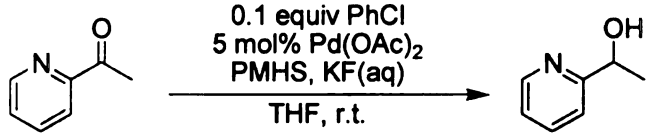
Following general procedure C in the absence of an aromatic chloride, with 1.5 equiv of PMHS (4 mmol, 0.24 mL) and 4 equiv KF (4 mmol, 0.232 g), 2,2-dimethyl-1-phenyl-propan-1-one (1 mmol, 0.167 mL) was reduced, affording 0.160 g (96%) of 2,2-dimethyl-1-phenyl-propan-1-ol.



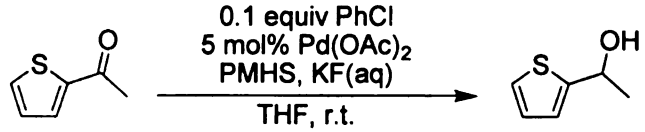
Following general procedure C 2-acetylmesitlyene (1 mmol, 0.166 mL) could not be reduced, with 97.5% of the S.M. being recovered.



Following general procedure C 2-acetylfurane (1 mmol, 0.100 mL) was reduced, affording 2-ethylfuran in 100% yield, as determined by ^{1}H NMR (d1 = 1, nt = 32) in d8-THF with CH_2Cl_2 (1 mmol, 0.064 mL) as an internal standard; 5.22 ppm (CH_2Cl_2, set to 2 H), 1.14 ppm (CH_3 for Furyl-Et, measured 3H, 100%).

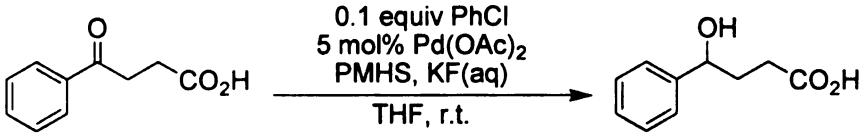


Following general procedure C 2-acetylpyridine (1 mmol, 0.112 mL) was reduced, affording 1-(pyridin-2-yl)ethanol in 98% yield, as determined by ^{1}H NMR (d1 = 1, nt = 32) in d8-THF with CH_2Cl_2 (1 mmol, 0.064 mL) as an internal standard; 5.22 ppm (CH_2Cl_2, set to 2 H), 1.34 (CH_3 for py-CH(OH)CH_3, measured 2.93H, 97.7%).



Following general procedure C 2-acetylthiophene (1 mmol, 0.108 mL) was reduced, affording 1-(thiophen-2-yl)ethanol in 23% yield, as determined by ^{1}H NMR (d1 = 1, nt = 32) in d8-THF with CH_2Cl_2 (1 mmol, 0.064 mL) as an internal

standard; 5.22 ppm (CH_2Cl_2, set to 2 H), 2.44 (CH_3 for Ac, measured 2.3H, 76.5% S.M.) 1.40 (CH_3 for thiophene-CH(OH)CH_3, measured 0.70H, 23.4%).



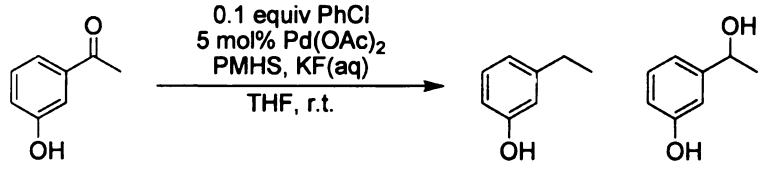
Following general procedure C 3-benzoylpropionic acid (1 mmol, 0.178 g) was reduced, affording 4-phenylbutanoic acid (9%) and 4-hydroxy-4-phenylbutanoic acid (91%) contaminated with silicon byproduct that could not be removed.

Following general procedure C in the absence of an aromatic chloride, with 1.5 equiv of PMHS (1.5 mmol, 0.09 mL) and 2 equiv of KF (2 mmol, 0.116 g), 3-benzoylpropionic acid (1 mmol, 0.178 g) was reduced affording 0.1657 g (92%) of 4-hydroxy-4-phenylbutanoic acid as a white solid; mp = 80 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.24 (m, 5H), 5.91 (bs, 2H), 4.63 (t, J = 6.59 Hz, 1 H), 2.33 (t, J = 7.14 Hz, 2H), 1.96 (m, 2H); ^{1}H NMR spectral data were consistent with literature.[136]

Following general procedure C 4'-hydroxyacetophenone (1mmol, 0.136 g) was reduced, affording 0.105 g (86%) of 4-ethyl-phenol as a white crystalline solid (silica gel FC, hexanes/EtOAc: 95/5 then 80/20); m.p. = 38-40 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.06 (d, J = 7.14 Hz, 2H), 6.78 (d, J = 7.14 Hz, 2H), 5.57 (s, 1H), 2.59 (q, J = 6.49 Hz, 2H), 1.21 (t, J = 6.49 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ

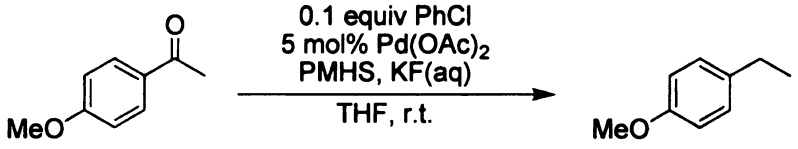
153.2, 136.5, 128.8, 115.1, 27.9, 15.8. Physical and spectral data were consistent with commercially available material.

Following general procedure C in the absence on an aromatic chloride, with 1.5 equiv of PMHS (1.5 mmol, 0.09 mL) and 2 equiv KF (2 mmol, 0.116 g), 4'-hydroxyacetophenone (1mmol, 0.136 g) was reduced, affording 0.0922 g (67%) of 4-(1-hydroxy-ethyl)-phenol as a white crystalline solid and 0.0544 g (40%) S.M. (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 140 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + D6-DMSO), δ 8.51 (s, 1H), 6.92 (d, J = 7.14 Hz, 2H), 6.51 (d, J = 7.14 Hz, 2H), 4.48 (m, 1H), 4.04 (s, 1H), 1.14 (d, J = 7.49 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + D6-DMSO), δ 155.6, 136.7, 126.0, 114.4, 68.5, 24.7. Physical and spectral data were consistent with those previously reported.[137]

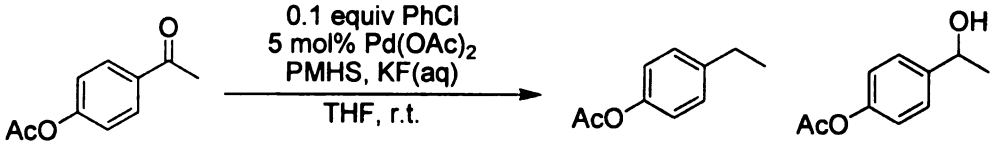


Following general procedure C 1 3'-hydroxyacetophenone (1 mmol, 0.136 g) was reduced, affording 0.0413 g (34%) of 3-ethyl-phenol, and 0.0693 g (50%) of 3-(1-hydroxy-ethyl)-phenol (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); (3-ethyl-phenol) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.13 (t, J = 7.69 Hz, 1H), 6.76 (d, J = 7.69 Hz, 1H), 6.64 (m, 2H), 5.05 (s, 1H), 2.59 (q, J = 7.69 Hz, 2H), 1.21 (t, J = 7.69 Hz, 3H); spectral data were consistent with commercially available material; (3-(1-hydroxy-ethyl)-phenol); mp = 112-114 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + D6-DMSO), δ 8.53 (s, 1H), 6.88 (t, J = 7.69 Hz, 1H), 6.63 (s, 1H), 6.58 (d, J = 7.69 Hz, 1H), 6.45 (d, J = 8.24 Hz, 1H), 4.51 (m, 1H), 4.05 (s, 1H), 1.17 (d, J = 6.04

Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + D6-DMSO), δ 156.6, 147.8, 128.6, 115.9, 113.4, 112.0, 68.8, 24.8. Physical and spectral data were consistent with literature.[138]

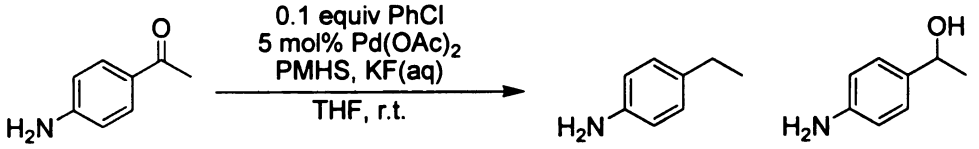


Following general procedure C 4-methoxyacetophenone (1 mmol, 0.15 g) was reduced, affording 0.1288 g (94.6%) of 4-ethyl-anisol as a clear liquid (silica gel FC, hexanes/EtOAc: 95/5); ^1H NMR (300 MHz, $CDCl_3$), δ 7.15 (d, J = 8.79 Hz, 2H), 6.86 (d, J = 8.79 Hz, 2H), 3.81 (s, 3H), 2.63 (q, J = 7.69 Hz, 2H), 1.24 (t, J = 7.69 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 157.5, 136.3, 128.6, 113.6, 55.1, 27.9, 15.8; spectral data were consistent with commercially available material.

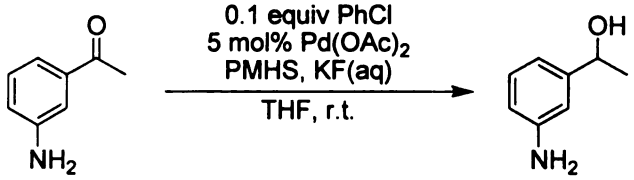


Following general procedure C, 4-acetoxy-acetophenone (1 mmol, 0.178 g) was reduced, affording 0.0086 g (5.2%) of 4-ethylphenyl-acetate, and 0.1686 g (93.5%) of 1-(4-acetoxy-phenyl)-ethanol as a light yellow oil (silica gel FC, hexanes/EtOAc: 80/20); (4-ethylphenyl-acetate) ^1H NMR (300 MHz, $CDCl_3$), δ 7.17 (d, J = 8.24 Hz, 2H), 6.96 (d, J = 8.24 Hz, 2H), 2.62 (q, J = 7.69 Hz, 2H), 2.27 (s, 3H), 1.21 (t, J = 7.69 Hz, 3H); (1-(4-acetoxy-phenyl)-ethanol) ^1H NMR (300 MHz, $CDCl_3$), δ 7.29 (d, J = 8.24 Hz, 2H), 6.98 (d, J = 8.24 Hz, 2H), 4.78 (q, J = 6.59 Hz, 1H), 2.72 (bs, 1H), 2.23 (s, 3H), 1.39 (d, J = 6.59 Hz, 3H); ^{13}C NMR

(75 MHz, $CDCl_3$), δ 169.5, 149.5, 143.3, 126.3, 121.2, 69.4, 24.9, 14.0; physical and spectral data were consistent with those previously reported.[137]

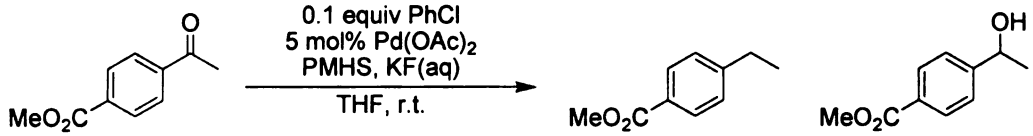


Following general procedure C 4'-aminoacetophenone (1 mmol, 0.135 g) was reduced, affording 0.0198 g (16%) of 4-ethyl-aniline as a red liquid, 0.0946 g (69%) of 1-(4-amino-phenyl)-ethanol as a red liquid, and 0.0204 g (15%) of S.M. (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); (4-ethyl-aniline) ^1H NMR (300 MHz, $CDCl_3$), δ 6.97 (d, J = 8.24 Hz, 2H), 6.61 (d, J = 8.24 Hz, 2H), 3.36 (bs, 2H), 2.52 (q, J = 7.41, 2H), 1.17 (t, J = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 143.9, 134.4, 128.5, 115.2, 277.9, 15.9; (1-(4-amino-phenyl)-ethanol) ^1H NMR (300 MHz, $CDCl_3$), δ 7.10 (d, J = 8.79 Hz, 2H), 6.59 (d, J = 8.24 Hz, 2H), 4.72 (q, J = 6.59 Hz, 1H), 3.19 (bs, 3H), 1.40 (d, J = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 145.5, 135.9, 126.4, 114.9, 69.8, 24.7; spectral data were consistent with commercially available material.



Following general procedure C 1 3'-aminoacetophenone (1 mmol, 0.135 g) was reduced, affording 0.0504 g (36%) of 1-(3-amino-phenyl)-ethanol as an orange solid, and 0.0808 g (59.8%) of S.M. (silica gel FC, hexanes/EtOAc: 80/20); ^1H NMR (300 MHz, $CDCl_3$), δ 7.11 (t, J = 7.14 Hz, 1H), 6.71 (m, 2H), 6.57 (d, J =

7.14 Hz, 1H), 4.77 (q, J = 7.69 Hz, 1H), 3.05 (bs, 3H), 1.43 (d, J = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 147.2, 146.4, 129.4, 115.6, 114.2, 111.9, 70.3, 24.9; spectral data were consistent with commercially available material.



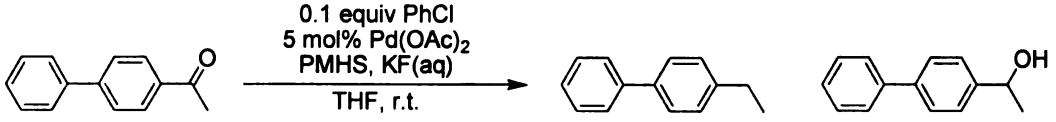
Following general procedure C 4-acetyl-methyl benzoate (1 mmol, 0.178 g) was reduced, affording 0.035 g (21%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1418 g (77%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); (4-ethyl-benzoic acid methyl ester) ^1H NMR (300 MHz, $CDCl_3$), δ 7.92 (d, J = 8.24 Hz, 2H), 7.22 (d, J = 8.24 Hz, 2H), 3.87 (s, 3H), 2.65 (q, J = 7.69 Hz, 2H), 1.22 (t, J = 7.69 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 167.1, 149.6, 129.6, 127.8, 127.5, 51.8, 28.8, 15.1; IR (neat) 2968, 2876, 1724, 1612, 1435, 1278, 1178, 1109 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0839. [4-(1-hydroxy-ethyl)-benzoic acid methyl ester] ^1H NMR (300 MHz, $CDCl_3$), δ 7.88 (d, J = 8.24 Hz, 2H), 7.32 (d, J = 8.24 Hz, 2H), 4.83 (q, J = 6.59 Hz, 1H), 3.81 (s, 3H), 2.89 (bs, 1H), 1.39 (d, J = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 167.0, 151.0, 129.6, 128.8, 125.1, 69.6, 52.0, 25.0; IR (neat) 3431, 2974, 2930, 1722, 1612, 1437, 1280, 1194, 1115, 1089, 1018, 900, 858 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{10}H_{12}O_3$ 180.0786, found 180.0784.

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL) and 4 equiv of KF (4 mmol, 0.232 g), 4-acetyl-methyl benzoate (1 mmol, 0.178 g) was

reduced affording 0.0418 g (25%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1317 g (73%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

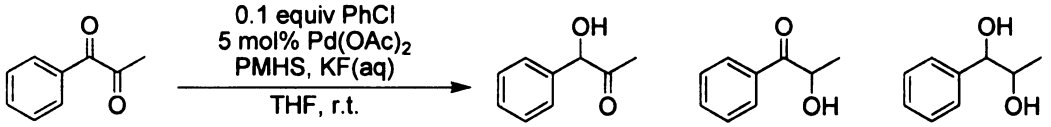
Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 4 equiv of KF (4 mmol, 0.232 g), and 0.1 equiv of TMS-Cl (0.1 mmol, 0.012 mL), 4-acetyl-methyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0418 g (25%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.1280 g (71%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.

Following general procedure C with 4 equiv of PMHS (4 mmol, 0.24 mL), 4 equiv of KF (4 mmol, 0.232 g), and 0.1 equiv of 4-chloroanisole (0.1 mmol, 0.012 mL), 4-acetyl-methyl benzoate (1 mmol, 0.178 g) was reduced affording 0.0858 g (52%) of 4-ethyl-benzoic acid methyl ester as a clear oil, and 0.0835 g (46%) of 4-(1-hydroxy-ethyl)-benzoic acid methyl ester as a yellow oil.



Following general procedure C 4-acetylbiphenyl (1 mmol, 0.196 g) was reduced, affording 0.1314 g (72%) of 4-ethyl-biphenyl as a clear solid, and 0.0477 g (24%) of 1-biphenyl-4-yl-ethanol as a yellow solid (silica gel FC, hexanes/EtOAc: 95/5 then 50/50); (4-ethyl-biphenyl); mp = 147 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.67 (d, *J* = 7.14 Hz, 2H), 7.61 (d, *J* = 8.24 Hz, 2H), 7.51 (d, *J* = 7.49, 2H), 7.42 (d, *J* = 7.14, 1H), 7.36 (d, *J* = 8.24 Hz, 2H), 2.78 (q, *J* = 7.69 Hz, 2H), 1.36 (t, *J* = 7.49 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 143.3, 141.1, 138.5, 128.6, 128.2, 127.0,

126.9, 126.9, 28.4, 15.5; (1-biphenyl-4-yl-ethanol); mp = 95 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.58 (d, *J* = 8.24 Hz, 4H), 7.44 (m, 4H), 7.34 (t, *J* = 7.14 Hz, 1H), 4.94 (q, *J* = 6.41, 1H), 1.94 (s, 1H), 1.53 (d, *J* = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 144.7, 140.8, 140.4, 128.7, 127.2, 127.0, 125.8, 70.0, 25.1; physical and spectral data were consistent with commercially available material.

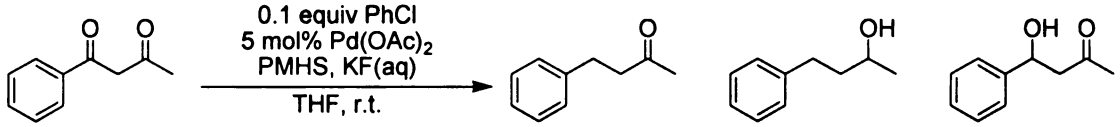


Following general procedure C 1-phenyl-1,2-propanedione (1 mmol, 0.134 mL) was reduced, affording 0.0726 g (48%) of 1-hydroxy-1-phenyl-propan-2-one as a light yellow liquid, and 0.0746 g (49%) of 1-phenyl-propane-1,2-diol as a mixture of anti and syn isomers (anti / syn = 2.6 / 1) (silica gel FC, hexanes/EtOAc: 95/5 then 95/5, 90/10, 80/20, then 50/50); (1-hydroxy-1-phenyl-propan-2-one) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.31 (m, 5H), 5.06 (s, 1H), 4.29 (bs, 1H), 2.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 207.0, 137.8, 129.3, 128.9, 128.7, 128.5, 127.3, 80.1, 25.2; physical and spectral data were consistent with those previously reported;[139] (1-phenyl-propane-1,2-diol) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.29 (m, 5H), 4.62 (d, *J* = 3.84 Hz, 0.73H), 4.28 (d, *J* = 7.69 Hz, 0.28H), 3.93 (dq, *J* = 2.19, 6.59 Hz, 0.73H), 3.78 (q, *J* = 7.14 Hz, 0.31H), 3.01 (bs, 2H), 0.99 (t, *J* = 7.41 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 141.0, 140.3, 128.3, 128.2, 127.9, 127.6, 126.8, 126.5, 79.4, 77.4, 72.1, 71.2, 18.6, 16.8; physical and spectral data were consistent with those previously reported.[87]

Following general procedure C with 5 equiv of PMHS (5 mmol, 0.3 mL), 1-phenyl-1,2-propanedione (1 mmol, 0.134 mL) was reduced, affording 0.0509 g (34%) of 1-hydroxy-1-phenyl-propan-2-one and 2-hydroxy-1-phenyl-propan-1-one as a 2 / 1 mixture, 0.066 g (43%) of 1-phenyl-propane-1,2-diol as a mixture of anti and syn isomers (anti / syn = 3 / 1), and 17% conversion to propyl-benzene (determined by GC); (2-hydroxy-1-phenyl-propan-1-one) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.89 (d, J = 7.69 Hz, 2H), 7.58 (t, J = 7.69 Hz, 1H), 7.46 (t, J = 7.69 Hz, 2H), 5.12 (q, J = 6.59 Hz, 1H), 3.84 (s, 1H), 1.4 (d, J = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 202.2, 133.8, 133.1, 128.9, 128.6, 69.1, 22.1. physical and spectral data were consistent with those previously reported.[140]

Following general procedure C in the absence of an aromatic chloride, with 1.5 equiv of PMHS (1.5 mmol, 0.09 mL), and 2 equiv of KF (2 mmol, 0.116 g), 1-phenyl-1,2-propanedione (1 mmol, 0.134 mL) was reduced, affording 0.1115 g (74%) of 1-hydroxy-1-phenyl-propan-2-one and 2-hydroxy-1-phenyl-propan-1-one as a 2 / 1 mixture, and 0.0297 g (19%) of 1-phenyl-propane-1,2-diol as a mixture of anti and syn isomers (anti / syn = 1.5 / 1).

Following general procedure C in the absence of an aromatic chloride, with 4 equiv of PMHS (5 mmol, 0.24 mL), and 4 equiv of KF (4 mmol, 0.232 g), 1-phenyl-1,2-propanedione (1 mmol, 0.134 mL) was reduced affording 0.0869 g (57.9%) of 1-hydroxy-1-phenyl-propan-2-one and 2-hydroxy-1-phenyl-propan-1-one as a 3 / 1 mixture, and 0.0484 g (31.8%) of 1-phenyl-propane-1,2-diol as a mixture of anti and syn isomers (anti / syn = 1.7 / 1).



Following general procedure C 1-phenyl-1,3-butanedione (1 mmol, 0.162 g) was reduced, affording 0.0111 g (7.48%) of 4-phenyl-butan-2-one, 0.0171 g (11.38%) of 4-phenyl-butan-2-ol, 0.0789 g (48.04%) of 4-hydroxy-4-phenyl-butan-2-one, 0.0211 g (14.07%) of 1-phenyl-butan-1-ol, 0.0135 g (8.12%) of 1-phenyl-butane-1,3-diol, and 0.0135 g (8.37%) of S.M.; (4-phenyl-butan-2-one) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.11 (m, 2H), 7.04 (m, 3H), 2.73 (t, J = 7.14 Hz, 2H), 2.62 (t, J = 7.14 Hz, 2H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 207.9, 140.9, 128.4, 128.2, 126.0, 45.1, 30.0, 29.6; (4-phenyl-butan-2-ol) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.20 (m, 5H), 3.80 (sep, J = 6.04 Hz, 1H), 2.70 (m, 2H), 1.75 (m, 3H), 1.21 (d, J = 6.04 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 142.0, 128.3, 125.7, 67.4, 40.8, 32.0, 23.5; physical and spectral data were consistent with commercially available material; (4-hydroxy-4-phenyl-butan-2-one) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.30 (m, 5H), 5.11 (dd, J = 3.29 and 8.79 Hz, 1H), 3.29 (bs, 1H), 2.80 (ddd, J = 3.84, 8.79 and 17.58 Hz, 2H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 209.0, 142.6, 128.4, 127.6, 125.5, 69.7, 51.9, 30.7; physical and spectral data were consistent with literature;[141] (1-phenyl-butan-1-ol) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.18 (m, 5H), 4.52 (t, J = 6.59 Hz, 1H), 1.72 (bs, 1H), 1.69 – 1.46 (m, 2H), 1.35 – 1.05 (m, 2H), 0.78 (t, J = 7.41 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 144.8, 128.3, 127.4, 125.8, 74.3, 41.1, 19.0, 13.9; physical and spectral data were consistent with commercially available material; (1-phenyl-butane-1,3-diol) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.34 (m, 5H), 4.92 (dd, J = 3.29, 9.88 Hz, 1H), 4.13

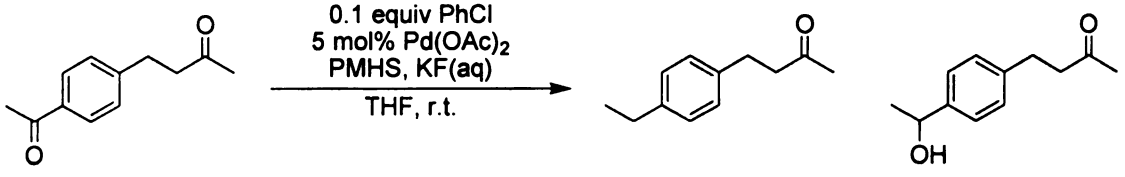
(m, 1H), 2.43 (bs, 2H), 1.82 (m, 2H), 1.20 (d, J = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 144.4, 128.5, 127.6, 125.6, 68.8, 47.0, 27.5, 24.0; physical and spectral data were consistent with literature.[142]

Following general procedure C with 5 equiv of PMHS (5mmol, 0.3 mL), 1-phenyl-1,3-butanedione (1 mmol, 0.162 g) was reduced, affording 0.0193 g (14.37%) of butyl-benzene, 0.0486 g (32.79%) of 4-phenyl-butan-2-one, 0.0698 g (46.52%) of 4-phenyl-butan-2-ol, 0.002 g (1%) of 1-phenyl-butan-1-ol, 0.003 g (1.8%) of 1-phenyl-butane-1,3-diol; (butyl-benzene) ^1H NMR (300 MHz, $CDCl_3$), δ 7.26 (m, 2H), 7.17 (m, 3H), 2.60 (t, J = 7.69 Hz, 2H), 1.59 (t, J = 7.69 Hz, 2H), 1.34 (m, 2H), 0.91 (t, J = 7.41 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 142.9, 128.4, 128.2, 125.6, 35.7, 33.7, 22.4, 13.9; physical and spectral data were consistent with commercial available material.

Following general procedure C in the absence of an aromatic chloride, with 1.5 equiv of PMHS (1.5 mmol, 0.09 mL) and 2 equiv of KF (2 mmol, 0.116 g), 1-phenyl-1,3-butanedione (1 mmol, 0.162 g) was reduced, affording 0.083 g (50.5%) of 4-hydroxy-4-phenyl-butan-2-one and 3-hydroxy-1-phenyl-butan-1-one as a 4.6 / 1 mixture, 0.006 g (3.61%) of 1-phenyl-butane-1,3-diol, and 0.0742 g (45.74%) of S.M.; (3-hydroxy-1-phenyl-butan-1-one) ^1H NMR (300 MHz, $CDCl_3$), δ 7.92 (d, J = 7.69 Hz, 2H), 7.56 (t, J = 7.69 Hz, 1H), 7.44 (t, J = 7.69 Hz, 2H), 4.43 – 4.31 (m, 1H), 3.36 (bs, 1H), 3.16 (dd, J = 3.01 and 17.58 Hz, 1H), 3.03 (dd, J = 8.79 and 17.58 Hz, 1H), 1.26 (d, J = 6.04 Hz, 3H); ^{13}C NMR (75 MHz,

$CDCl_3$), δ 200.7, 136.6, 133.4, 128.6, 128.0, 63.9, 46.4, 22.3; physical and spectral data were consistent with literature.[143]

Following general procedure C in the absence of an aromatic chloride, with 4 equiv of PMHS (4 mmol, 0.24 mL) and 4 equiv of KF (4 mmol, 0.232 g), 1-phenyl-1,3-butanedione (1 mmol, 0.162 g) was reduced, affording 0.0697 g (42.46%) of 4-hydroxy-4-phenyl-butan-2-one and 3-hydroxy-1-phenyl-butan-1-one as a 5.05 / 1 mixture, 0.0149 g (8.98%) of 1-phenyl-butane-1,3-diol, and 0.0776 g (47.84%) of S.M.

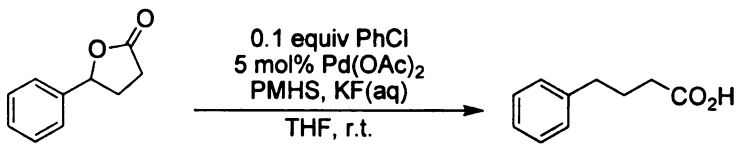


Following general procedure C 4-(4-acetyl-phenyl)-butan-2-one (1 mmol, 0.19 g) was reduced, affording 0.0925 g (52.5%) of 4-(4-ethyl-phenyl)-butan-2-one as a clear liquid, and 0.0846 g (44%) of 4-[4-(1-hydroxy-ethyl)-phenyl]-butan-2-one as a clear liquid: (4-(4-ethyl-phenyl)-butane-2-one) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.10 (s, 4H), 2.83 (t, *J* = 8.24 Hz, 2H), 2.75 (t, *J* = 8.24 Hz, 2H), 2.60 (q, *J* = 7.69 Hz, 2H), 2.12 (s, 3H), 1.21 (t, *J* = 7.69 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 208.0, 141.9, 138.0, 128.1, 127.9, 45.2, 30.0, 29.2, 28.3, 15.5; IR (neat) 3009, 2964, 2932, 2872, 1716, 1516, 1440, 1410, 1363, 1159, 819 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{12}H_{16}O$ 176.1201, found 176.1196. (4-[4-(1-hydroxy-ethyl)-phenyl]-butan-2-one) ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.24 (d, *J* = 8.24 Hz, 2H), 7.11 (d, *J* = 8.24 Hz, 2H), 4.78 (q, *J* = 6.59 Hz, 1H), 2.83 (t, *J* = 7.14 Hz, 2H), 2.71 (t, *J* = 6.86 Hz, 2H), 2.38 (bs, 1H), 2.09 (s, 3H), 1.42 (d, *J* = 6.59 Hz, 3H);

^{13}C NMR (75 MHz, $CDCl_3$), δ 208.0, 143.6, 139.8, 128.1, 125.4, 69.8, 44.9, 29.8, 29.1, 24.9; IR (neat) 3420, 2972, 1709, 1385, 1089, 898, 821 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{12}H_{16}O_2$ 192.1150, found 192.1149.

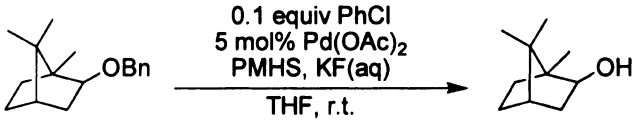
Following general procedure C with 4 equiv PMHS (4 mmol, 0.24 mL) and 0.1 equiv 4-chloroanisole (0.1 mmol, 0.012 mL), 4-(4-acetyl-phenyl)-butan-2-one (1 mmol, 0.19 g) was reduced affording 0.1275g (72%) of 4-(4-ethyl-phenyl)-butan-2-one as a clear liquid, and 0.0481 g (25%) of 4-[4-(1-hydroxy-ethyl)-phenyl]-butan-2-one as a clear liquid.

Following general procedure C in the absence of an aromatic chloride, with 3 equiv PMHS (3 mmol, 0.18 mL) and 4 equiv KF (4 mmol, 0.232 g), 4-(4-acetyl-phenyl)-butan-2-one (1 mmol, 0.19 g) was reduced affording 0.1812 g (94.2%) of 4-[4-(1-hydroxy-ethyl)-phenyl]-butan-2-one as a clear liquid, and 0.007 g (4%) of S.M..

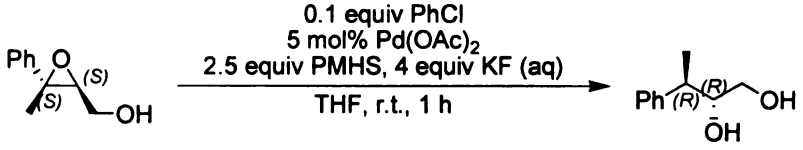


Following general procedure C with 1.5 eq. PMHS (1.5 mmol, 0.09 mL), and 2 eq. KF (2 mmol, 0.116 g) γ-phenyl-γ-butyrolactone (1 mmol, 0.162g) was reacted, affording 0.1477 g (90%) of 4-phenyl-butyric acid as a white solid (>90% purity), and 0.1114 g (68%) analytically pure material after a second column; m.p. 53 °C; ^1H NMR (300 MHz, $CDCl_3$), δ 10.91 (bs, 1H), 7.29 (m, 2H), 7.20 (m, 3H), 2.67 (t, *J* = 7.41 Hz, 2H), 2.37 (t, *J* = 7.41 Hz, 2H), 1.97 (q, *J* = 7.69 Hz, 2H); ^{13}C NMR

(75 MHz, $CDCl_3$), δ 180.0, 141.1, 128.4, 128.3, 125.9, 34.8, 33.2, 26.1. Physical and spectral data were consistent with commercially available material.

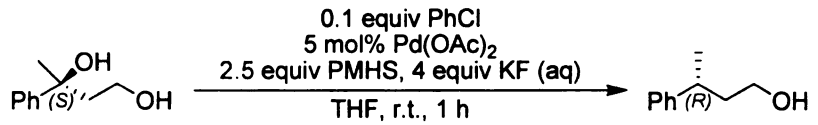


Following general procedure C benzyl bornyl ether (1 mmol, 0.244g) was reduced, affording 0.1028g (67%) of borneol as a white sold; m.p. = 200-204 °C; ^1H NMR (300 MHz, $CDCl_3$), δ 3.58 (dd, *J* = 2.19, 6.59 Hz, 1H), 1.76-1.38 (m, 6H), 0.98 (s, 3H), 0.95-0.9 (m, 1H), 0.87 (s, 3H), 0.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 79.8, 48.9, 46.2, 44.9, 40.3, 33.8, 27.5, 27.1, 20.4, 20.0, 11.3. Physical and spectral data were consistent with commercially available material.



Following general procedure C (2S,3S)-epoxy-3-phenyl-butan-1-ol (1 mmol, 0.164g, 89.5%ee) was reduced, affording 0.1614g (97.1%) of (2R,3R)-3-phenyl-butane-1,2-diol as a clear oil, and trace amounts of 3-phenyl-butan-1-ol: ^1H NMR (300 MHz, $CDCl_3$), δ 7.26 (m, 2H), 7.15 (m, 3H), 3.78 (bs, 1H), 3.67 (m, 2H), 3.33 (m, 1H), 3.24 (m, 1H), 2.70 (q, *J* = 7.41 Hz, 1H), 1.30 (d, *J* = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 143.7, 128.4, 127.8, 126.4, 76.5, 64.9, 42.7, 17.59; %de determined by GC using a Beta DEX™ 325 Fused Silica Capilary Column: 30mX0.25mmX0.25μm film thickness. GC conditions: starting temperature (30 °C), ramp rate (10 °C/min.), final temperature (200 °C for 15 min.), R.T. 20.17

(2.435%), 20.93 (97.565%), 95.13% de. Spectral data was identical to literature[144].



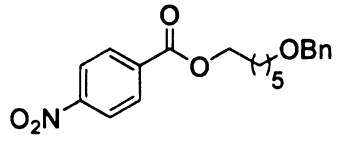
Following general procedure C (R)-3-phenyl-butane-1,3-diol (1 mmol, 0.166 g, 82.8%ee) was reduced, affording 0.0926 g (61.6%) of (3S)-3-Phenyl-butan-1-ol, and 0.0637 g (38.3%) of S.M.; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.29 (m, 2H), 7.21 (m, 3H), 3.52 (m, 2H), 2.87 (m, 1H), 1.84 (q, *J* = 6.59 Hz, 2H), 1.69 (bs, 1H), 1.26 (d, *J* = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 146.7, 128.4, 126.8, 126.0, 61.0, 40.8, 36.3, 22.3. Spectral data were consistent with commercially available material; %ee and absolute configuration was determined by derivativazation of the alcohol with (R)-MPA. A dry 10 mL round bottom was charged with 1.1 eq. of (R)-(-)-α-methoxyphenylacetic acid (0.4305 mmol, 0.0715g), and 3 crystals of DMAP. The round bottom was sealed and placed under an atmosphere of nitrogen. Freshly distilled CH_2Cl_2 (2 mL), (3S)-3-phenyl-butan-1ol (0.3914 mmol, 0.0588 g) in 0.5 mL CH_2Cl_2, and DCC (0.4305 mmol, 1.0M in CH_2Cl_2, 0.4305 mL) were injected sequentially and the reaction was stirred over night. The white precipitate was filtered off and rinsed with CH_2Cl_2. The filtrate was washed with 5% HCl (aq), sat. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to FC with hexanes/ethyl acetate (95/5 then 80/20) affording 0.1095 g (93%) of methoxy-phenyl-acetic acid 3-phenyl-butyl ester as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.46-7.31 (m, 5H), 7.25-7.08 (m, 3H), 7.04 (d, *J* = 7.14 Hz, 0.17H), 6.94 (d, *J* = 6.59 Hz, 1.83H), 4.69 (s, 1H), 4.03 (m, 1H),

3.89 (m, 1H), 3.38 (s, 3H), 2.62 (m, 1H), 1.82 (m, 2H), 1.18 (d, *J* = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 170.5, 145.7, 136.3, 128.7, 128.6, 128.4, 127.2, 126.8, 126.1, 82.4, 63.5, 57.2, 36.6, 36.2, 22.0; IR (neat) 3028, 2961, 2930, 2828, 1747, 1495, 1451, 1257, 1174, 1111, 1024, 700 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{19}H_{22}O_3$ 298.1569, found 298.1564.

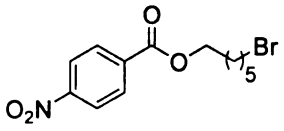
To insure that the chiral (R)-MPA ester formed could effect separation of the R and S enantomer of 3-phenyl-butan-1-ol, a racemic mixture of 3-phenyl-butan-1-ol (0.2735 mmol, 0.041 g) was coupled with (R)-MPA following the procedure above: ^1H NMR (300 MHz, $CDCl_3$), δ 7.48-7.31 (m, 5H), 7.28-7.09 (m, 3H), 7.05 (d, *J* = 7.14 Hz, 1H), 6.94 (d, *J* = 6.59 Hz, 1H), 4.70 (s, 1H), 4.10-3.83 (m, 2H), 3.39 (s, 1.5H), 3.38 (s, 1.5H), 2.61 (m, 1H), 1.82 (m, 2H), 1.19 (d, *J* = 7.14 Hz, 1.5H), 1.15 (d, *J* = 6,59 Hz, 1.5H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 170.5, 145.9, 145.7, 136.3, 128.6, 128.5, 128.4, 128.3, 127.2, 127.1, 126.7, 126.1, 82.5, 82.4, 63.5, 57.2, 36.6, 36.2, 36.2, 22.0, 21.9.

Chapter 5 Experimental

Procedures for the Preparation of Starting Material Found in Chapter 5

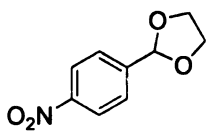


Procedure for the preparation of 6-(benzyloxy)hexyl 4-nitrobenzoate: A flame dried 100 mL round bottom under a nitrogen atmosphere was charged with 4-nitrobenzoic acid (20 mmol, 3.34 g), 6-(benzyloxy)hexan-1-ol[145] (20 mmol, 4.16 g), *N,N*-dimethylaminopyridine (4 mmol, 0.49 g), and 20 mL of dry CH_2Cl_2. DCC (1 M in CH_2Cl_2, 30 mmol, 30 mL) was injected into the round bottom slowly and the reaction was stirred overnight (14 h). The reaction mixture was filtered and the solid white material rinsed with CH_2Cl_2. The filtrate was sequentially washed with 10% HCl (aq) and sat. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/EtOAc: 95/5) affording 5.51 g (77%) of 6-(benzyloxy)hexyl 4-nitrobenzoate as a pale yellow solid; m.p. = 38-40 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (d, *J* = 8.79 Hz, 2H), 8.15 (d, *J* = 8.79 Hz, 2H), 7.29 (m, 5H), 4.47 (s, 2H), 4.33 (t, *J* = 6.59 Hz, 2H), 3.45 (t, *J* = 6.59 Hz, 2H), 1.77 (m, 2H), 1.63 (m, 2H), 1.44 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.6, 150.4, 138.5, 135.8, 130.6, 128.3, 127.5, 127.4, 123.4, 72.8, 70.1, 65.9, 29.6, 28.5, 25.9, 25.8; IR (Nujol) 1718, 1608, 1525, 1454, 1346, 1273, 1105, 873, 742, 715 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{20}H_{23}NO_5$ 357.1576, found 357.1580.



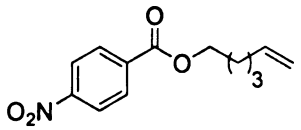
Procedure for the preparation of 6-bromohexyl 4-nitrobenzoate: A flame dried 250 mL round bottom was charged with 4-nitrobenzoic acid (60 mmol, 10 g), 1,6-hexanediol (180 mmol, 21.3 g), DMAP (12 mmol, 1.47 g), and 60 mL of dry CH_2Cl_2. The round bottom was sealed and purged with nitrogen. The flask was placed in an ice-bath and DCC (1M in CH_2Cl_2, 99 mmol, 99 mL) was added dropwise via a cannula. After complete addition of the DCC the reaction was stirred for an additional 20 minutes at the ice-bath temperature. The reaction was then allowed to warm to room temperature and stir over night (12 h). The reaction mixture was filtered and the solid material rinsed with CH_2Cl_2. The filtrate was washed with 0.5 N HCl and then saturated sodium bicarbonate solution. The organics were dried ($MgSO_4$), concentrated, and subjected to flash chromatography (hexanes/EtOAc: 90/10, 80/20, then 50/50) affording 13.63 g (85%) of 6-hydroxyhexyl 4-nitrobenzoate as a pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, J = 8.79 Hz, 2H), 8.15 (d, J = 8.79 Hz, 2H), 4.30 (t, J = 6.59 Hz, 2H), 3.61 (t, J = 6.59 Hz, 2H), 1.70 (quin, J = 6.59 Hz, 2H), 1.56 (quin, J = 6.59 Hz, 2H), 1.43 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 150.4, 135.7, 130.5, 123.4, 65.8, 62.6, 32.4, 28.4, 25.7, 25.3. This material (10 mmol, 2.67 g) was added to a dry 25 mL round bottom that had been charged with carbon tetrabromide (12.5 mmol, 4.14 g) and 15 mL of dry CH_2Cl_2. The reaction was placed in an ice-bath and a nitrogen line was placed in the neck of the round bottom and triphenylphosphine (15 mmol, 3.93 g) was added in four portions

over a period of 5 minutes. The reaction turned from a light yellow to a brown orange color after complete addition of the PPh_3. The reaction was stirred for 15 minutes, followed by evaporation to half volume. The mixture was then diluted with ether. The solid material was filtered off and rinsed with ether. The filtrate was concentrated and subjected to flash chromatography (hexanes/EtOAc: 90/10) affording 3.12 g (94%) of 6-bromohexyl 4-nitrobenzoate as light yellow solid; mp = 45–47 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.79 Hz, 2H), 8.17 (d, *J* = 8.79 Hz, 2H), 4.34 (t, *J* = 6.59 Hz, 2H), 3.39 (t, *J* = 6.59 Hz, 2H), 1.86 (quin, *J* = 7.14 Hz, 2H), 1.78 (quin, *J* = 7.14 Hz, 2H), 1.56–1.38 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.6, 150.4, 135.6, 130.6, 123.5, 65.7, 33.6, 32.4, 28.4, 27.7, 25.1; IR (THF solution) 3111, 3080, 3055, 2939, 1724, 1608, 1529, 1464, 1350, 1275, 1103, 1014, 873, 721 cm^{-1}; LRMS (EI, 70 eV) 250 (0.13), 167 (12), 164 (33), 162 (13), 161 (19), 150 (35), 149 (46), 133 (11), 135 (8), 137 (9), 120 (20), 104 (16), 103 (21), 92 (14), 82 (100), 75 (18), 76 (18), 67 (14), 55 (30), 54 (26), 41 (24); HRMS (EI) *m/z* calcd for $C_{13}H_{16}BrNO_4$ 329.0263, found 329.0258.



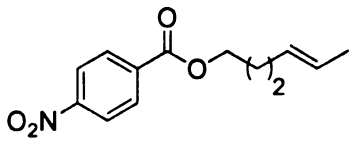
Procedure for the preparation of 2-(4-nitrophenyl)-1,3-dioxolane: A flame dried 500 mL round bottom was connected to a Dean-Stark trap with a reflux condenser and drying tube. The round bottom was charged with 4-nitrobenzaldehyde (30 mmol, 4.53 g), *p*-toluenesulfonic acid monohydrate (1.8 mmol, 0.34 g), ethylene glycol (600 mmol, 33.5 mL), and dry benzene (300 mL). The round bottom was placed in an oil-bath at 100 °C and the reaction was

refluxed for 8 hours. The reaction was cooled to room temperature then poured into a sep-funnel containing 10% aqueous potassium carbonate. The organic layer was dried over $MgSO_4$, filtered, and concentrated affording 3.89 g (66%) of clean 2-(4-nitrophenyl)-1,3-dioxolane as light yellow solid; mp = 88-91 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.79 Hz, 2H), 7.62 (d, *J* = 8.79 Hz, 2H), 5.86 (s, 1H), 4.07 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.3, 144.9, 127.4, 123.5, 102.2, 65.4; IR (PTFE card, neat) 1522, 1358, 1184, 1126, 1080, 846, 750, 667 cm^{-1}. Spectral data were consistent with those previously reported.[146]

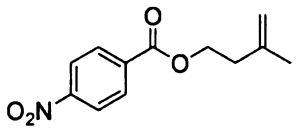


Procedure for the preparation of hex-5-enyl 4-nitrobenzoate: A flame dried 100 mL round bottom under a nitrogen atmosphere was charged with 4-nitrobenzoic acid (20 mmol, 3.34 g), 5-hexen-1-ol (40 mmol, 4.81 mL), *N,N*-dimethylaminopyridine (4 mmol, 0.49 g), and 20 mL of dry CH_2Cl_2. DCC (1 M in CH_2Cl_2, 24 mmol, 24 mL) was injected into the round bottom slowly and the reaction was stirred overnight (14 h). The reaction mixture was filtered and the solid white material rinsed with CH_2Cl_2. The filtrate was sequentially washed with 10% HCl (aq) and sat. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/EtOAc: 95/5) affording 4.31 g (86.5%) of yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.79 Hz, 2H), 8.16 (d, *J* = 8.79 Hz, 2H), 5.78 (m, 1H), 4.96 (m, 2H), 4.34 (t, *J* = 7.14 Hz, 2H), 2.10 (q, *J* = 7.14 Hz, 2H), 1.78 (m, 2H), 1.51 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.4, 138.0, 135.7, 130.6, 123.4, 114.9, 65.8, 33.2, 27.9,

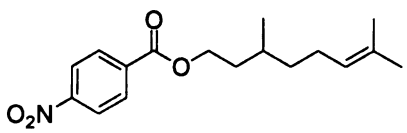
25.1; IR (neat) 2939, 1726, 1529, 1350, 1277, 1118, 1103, 1014, 914, 873, 719 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{13}H_{15}NO_4 + H]^+$ 250.1079, found 250.1085.



Procedure for the preparation of (E)-hex-4-enyl 4-nitrobenzoate: A flame dried 100 mL round bottom under a nitrogen atmosphere was charged with 4-nitrobenzoic acid (20 mmol, 3.34 g), 4-hexen-1-ol (24 mmol, 2.8 mL), *N,N*-dimethylaminopyridine (4 mmol, 0.49 g), and 20 mL of dry CH_2Cl_2. DCC (1 M in CH_2Cl_2, 24 mmol, 24 mL) was injected into the round bottom slowly and the reaction was stirred overnight (14 h). The reaction mixture was filtered and the solid white material rinsed with CH_2Cl_2. The filtrate was sequentially washed with 10% HCl (aq) and sat. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/EtOAc: 95/5) affording 4.31 g (86.5%) of pale yellow solid; mp = 44 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.79 Hz, 2H), 8.17 (d, *J* = 8.79 Hz, 2H), 5.42 (m, 2H), 4.34 (t, *J* = 6.59 Hz, 2H), 2.11 (m, 2H), 1.82 (q, *J* = 6.59 Hz, 2H), 1.63 (d, *J* = 4.94 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.4, 135.7, 134.8, 130.6, 129.6, 126.1, 123.4, 65.4, 28.8, 28.3, 17.8; IR (Nujol) 1728, 1604, 1531, 1348, 1319, 1275, 1103, 968, 871, 843, 788, 717 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{13}H_{15}NO_4 + H]^+$ 250.1079, found 250.1077.

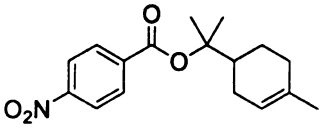


Procedure for the preparation of 3-methylbut-3-enyl 4-nitrobenzoate: A flame dried 100 mL round bottom under a nitrogen atmosphere was charged with 4-nitrobenzoic acid (20 mmol, 3.34 g), 3-methyl-3-buten-1-ol (40 mmol, 4.03 mL), *N,N*-dimethylaminopyridine (4 mmol, 0.49 g), and 20 mL of dry CH_2Cl_2. DCC (1 M in CH_2Cl_2, 24 mmol, 24 mL) was injected into the round bottom slowly and the reaction was stirred overnight (14 h). The reaction mixture was filtered and the solid white material rinsed with CH_2Cl_2. The filtrate was sequentially washed with 10% HCl (aq) and sat. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/EtOAc: 95/5) affording 3.05 g (64.9%) of yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, J = 8.79 Hz, 2H), 8.15 (d, J = 8.79 Hz, 2H), 4.79 (d, J = 13.18 Hz, 2H), 4.45 (t, J = 6.59 Hz, 2H), 2.46 (t, J = 6.59 Hz, 2H), 1.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.5, 150.4, 141.2, 135.6, 130.6, 123.4, 112.6, 63.8, 36.6, 22.3; IR (neat) 1716, 1522, 1348, 1284, 1103, 906, 871, 715 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{12}H_{13}NO_4 + H]^+$ 236.0923, found 236.0919.



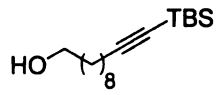
Procedure for the preparation of 3,7-Dimethyloct-6-enyl 4-nitrobenzoate: A flame dried 100 mL round bottom under a nitrogen atmosphere was charged with 4-nitrobenzoic acid (30 mmol, 5.01 g), β-citronellol (45 mmol, 8.18 mL), *N,N*-

dimethylaminopyridine (6 mmol, 0.73 g), and 30 mL of dry CH_2Cl_2. DCC (1 M in CH_2Cl_2, 45 mmol, 45 mL) was injected into the round bottom slowly and the reaction was stirred overnight (14 h). The reaction mixture was filtered and the solid white material rinsed with CH_2Cl_2. The filtrate was sequentially washed with 10% HCl (aq) and sat. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/CH_2Cl_2: 50/50) affording 7.82 g (85%) of yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.79 Hz, 2H), 8.16 (d, *J* = 8.79 Hz, 2H), 5.05 (t, *J* = 7.14 Hz, 1H), 4.37 (m, 2H), 1.97 (q, *J* = 7.69 Hz, 2H), 1.80 (m, 1H), 1.63 (s, 3H), 1.56 (s, 3H), 1.36 (m, 2H), 1.22 (m, 2H), 0.94 (d, *J* = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.6, 150.4, 135.8, 131.4, 130.6, 124.3, 123.4, 64.4, 36.9, 35.3, 29.5, 25.6, 25.3, 19.4, 17.6; IR (neat) 2963, 2926, 1726, 1608, 1529, 1456, 1350, 1277, 1116, 1103, 873, 835, 785, 719 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{17}H_{23}NO_4 + H]^+$ 306.1705, found 306.1700.



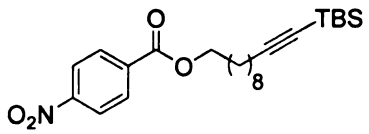
Procedure for the preparation of 2-(4-methylcyclohex-3-enyl)propan-2-yl 4-nitrobenzoate: A flame dried 100 mL round bottom under a nitrogen atmosphere was charged with 4-nitrobenzoic acid (20 mmol, 3.34 g), α-terpineol (40 mmol, 6.61 mL), *N,N*-dimethylaminopyridine (4 mmol, 0.49 g), and 20 mL of dry CH_2Cl_2. DCC (1 M in CH_2Cl_2, 40 mmol, 40 mL) was injected into the round bottom slowly and the reaction was stirred overnight (14 h). The reaction mixture was filtered and the solid white material rinsed with CH_2Cl_2. The filtrate was sequentially

washed with 10% HCl (aq) and sat. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/CH_2Cl_2: 50/50) affording 3.49 g (58%) of light yellow solid; mp = 140 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.22 (d, *J* = 8.79 Hz, 2H), 8.09 (d, *J* = 8.79 Hz, 2H), 5.35 (s, 1H), 2.21-1.78 (m, 7H), 1.62 (s, 3H), 1.58 (s, 3H), 1.55 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.5, 150.2, 137.4, 134.0, 130.4, 123.3, 120.0, 87.2, 43.0, 30.8, 26.4, 24.0, 23.3, 23.2; IR (PTFE card, neat) 3111, 3001, 2959, 2924, 2897, 2855, 1711, 1523, 1348, 1309, 1203, 1147, 1103, 924, 717cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{17}H_{21}NO_4 + H]^+$ 304.1549, found 304.1550.



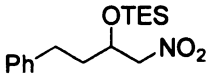
Procedure for the preparation of 11-(tert-butyldimethylsilyl)undec-10-yn-1-ol: A dry 1 L round bottom was placed in an ice-bath and charged with 10-undecyn-1-ol (67 mmol, 12.9 mL), 250 mL of dry THF, and 50 mL of *n*-BuLi (1.6 M in hexanes, 80 mmol). The reaction was stirred for 30 minutes then an additional 50 mL of *n*-BuLi (1.6 M in hexanes, 80 mmol) was added and the round bottom was removed from the ice-bath. TBS-Cl (80 mmol, 12.1 g) dissolved in 10 mL of THF was added in four portions with hand shacking the round bottom between each addition. The reaction was stirred for 10 hours then poured into a sep-funnel containing ether and water. The layers were separated, and the organic layer was dried over $MgSO_4$, filtered, concentrated, and subjected to flash chromatography (hexanes/ EtOAc: 80/20) affording 12.9 g (68%) of 11-(tert-butyldimethylsilyl)undec-10-yn-1-ol as a clear oil, and 5.51 g

(21%) of tert-butyl(11-(tert-butyldimethylsilyl)undec-10-ynyloxy)dimethylsilane as a clear oil; for 11-(tert-butyldimethylsilyl)undec-10-yn-1-ol: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.59 (m, 2H), 2.18 (t, *J* = 6.59 Hz, 2H), 1.58-1.16 (m, 14H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 108.2, 108.1, 82.1, 62.9, 32.7, 29.4, 29.3, 28.9, 28.6, 26.1, 25.9, 25.6, 19.7, 16.4, -4.4; IR (neat) 3321, 2937, 2856, 2174, 1471, 1250, 1055, 837, 773, 680 cm^{-1}

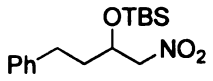


Procedure for the preparation of 11-(tert-butyldimethylsilyl)undec-10-ynyl 4-nitrobenzoate: A flame dried 100 mL round bottom under a nitrogen atmosphere was charged with 4-nitrobenzoic acid (20 mmol, 3.34 g), 11-(tert-butyldimethylsilyl)undec-10-yn-1-ol (22 mmol, 6.21 mL), *N,N*-dimethylaminopyridine (4 mmol, 0.49 g), and 20 mL of dry CH_2Cl_2. DCC (1 M in CH_2Cl_2, 30 mmol, 30 mL) was injected into the round bottom slowly and the reaction was stirred overnight (18 h). The reaction mixture was filtered and the solid white material rinsed with CH_2Cl_2. The filtrate was sequentially washed with 10% HCl (aq) and sat. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/EtOAc: 80/20) affording 7.86 g (91%) of 11-(tert-butyldimethylsilyl)undec-10-ynyl 4-nitrobenzoate as a clear light yellow oil. The oil was further purified by Kugelrohr distillation (225 °C at 0.1 mmHg) affording 7.10 g (82.3%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.79 Hz, 2H), 8.17 (d, *J* = 8.79 Hz, 2H), 4.33 (t, *J* = 7.14 Hz, 2H), 1.75 (q, *J* = 6.59 Hz, 2H), 1.54-1.21 (m, 12H), 0.88 (s, 9H), 0.04 (s, 6H);

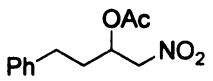
^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 150.4, 135.8, 130.6, 123.4, 108.0, 82.3, 66.0, 29.3, 29.1, 28.9, 28.6, 28.5, 26.0, 25.9, 19.7, 16.5, -4.4; IR (neat) 2930, 2856, 2172, 1728, 1531, 1471, 1350, 1275, 1120, 1103, 1014, 837, 775, 719 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{24}H_{37}NO_4Si + H]^+$ 432.2570, found 432.2575.



Procedure for the preparation of triethyl(1-nitro-4-phenylbutan-2-yloxy)silane: a dry 25 mL round bottom was charged with 1-nitro-4-phenylbutan-2-ol[147] (10 mmol, 1.95 g), imidazole (25 mmol, 1.70 g), and 5 mL of dry DMF. The round bottom was sealed and placed under an atmosphere of nitrogen, followed by injecting chlorotriethylsilane (12 mmol, 2.01 mL) into the reaction and stirring for 12 hours. The reaction was diluted with water and extracted with CH_2Cl_2. The aqueous layer was back extracted with CH_2Cl_2 and the combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/EtOAc: 95/5 then 80/20) affording 1.657 g (53.5%) of triethyl(1-nitro-4-phenylbutan-2-yloxy)silane as a dark yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.32-7.12 (m, 5H), 4.45 (m, 1H), 4.35 (m, 2H), 2.66 (m, 2H), 1.86 (m, 2H), 0.94 (t, *J* = 8.24 Hz, 9H), 0.58 (q, *J* = 8.24 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.9, 128.6, 128.1, 126.2, 80.9, 69.5, 36.9, 31.0, 6.6, 4.8; IR (neat) 2957, 2878, 1558, 1456, 1415, 1385, 1240, 1116, 1005, 733 cm^{-1}: HRMS (Methane Chem Ion) *m/z* calcd for $[C_{16}H_{27}NO_3Si + H]^+$ 310.1838, found 310.1829.

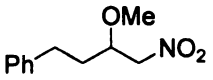


***tert*-Butyldimethyl(1-nitro-4-phenylbutan-2-yloxy)silane** was prepared following the procedure state above with *t*-butyldimethylchlorosilane (12 mmol, 1.81 g), affording after flash chromatography (hexanes/Et_2O: 100/0 then 85/15) 2.22 g (72%) of yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.34 (m, 5H), 4.51-4.30 (m, 3H), 2.67 (dt, *J* = 2.74, 7.69 Hz, 2H), 1.88 (m, 2H), 0.88 (s, 9H), 0.08 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.9, 128.6, 128.1, 126.2, 80.8, 69.5, 36.8, 30.8, 25.6, 17.9, -4.6, -5.1; IR (neat) 2955, 2930, 2858, 1556, 1471, 1387, 1257, 1115, 1003, 837, 779, 748, 700 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{16}H_{27}NO_3Si + H]^+$ 310.1838, found 310.1845.



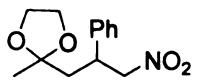
Procedure for the preparation of 1-nitro-4-phenylbutan-2-yl acetate: A dry 100 mL round bottom was charged with 1-nitro-4-phenylbutan-2-ol[143] (10 mmol, 1.95 g) and placed under an atmosphere of nitrogen. Freshly distilled CH_2Cl_2 (20 mL), pyridine (14 mmol, 1.13 mL), and acetyl chloride (12 mmol, 0.85 mL) were injected sequentially, and the reaction was stirred for 14 hours. The reaction mixture was quenched with sat. $NaHCO_3$, transferred to a sep-funnel, and the organic layer washed with brine. The organics were then dried over sodium sulfate, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/EtOAc: 95/5 then 80/20) affording 1.01 g (42.5%) of 1-nitro-4-phenylbutan-2-yl acetate as a yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.32-7.11 (m, 5H), 5.42 (m, 1H), 4.48 (m, 2H), 2.67 (m, 2H), 2.03 (s, 3H), 1.96

(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 140.0, 128.5, 128.1, 126.3, 77.1, 69.4, 32.9, 31.1, 20.6; IR (neat) 3028, 2932, 1747, 1558, 1375, 1230, 1047, 943, 752, 700 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{12}H_{15}NO_4 + H]^+$ 238.1079, found 238.1079.



Procedure[148] for the preparation of (3-methoxy-4-nitrobutyl)benzene: A dry 250 mL round bottom was charged with Proton-Sponge® (61.13 mmol, 13.1 g) and methyl trifluoromethanesulfonate (50.94 mmol, 5.76 mL), connected to a reflux condenser, and placed under a positive pressure of nitrogen. 1-Nitro-4-phenylbutan-2-ol[143] (10.19 mmol, 1.99 g) in 50 ml of freshly distilled chloroform were injected down the reflux condenser followed by 40 mL of freshly distilled chloroform. The nitrogen inlet was removed, the round bottom was placed in an oil-bath, and the reaction was refluxed for 14 hours. After cooling to room temperature 3 mL of concentrated ammonium hydroxide was added and the mixture was stirred for an additional 2 hours. The reaction mixture was poured into a sep-funnel containing water, extracted with CH_2Cl_2, and the organics washed with 10% HCl. The organics were dried over $MgSO_4$, filtered, and concentrated. The crude material was subjected to flash chromatography (hexanes/EtOAc: 90/10) affording 1.31 g (61%) of (3-methoxy-4-nitrobutyl)benzene as a light red-yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33-7.13 (m, 5H), 4.40 (m, 2H), 3.54 (m, 1H), 3.39 (s, 3H), 2.70 (m, 2H), 1.87 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.7, 128.5, 128.2, 126.2, 78.3, 77.3, 57.7,

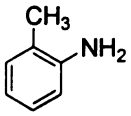
33.2, 30.9; IR (neat) 2936, 1558, 1456, 1387, 1116, 750, 700 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{11}H_{15}NO_3 + H]^+$ 210.1130, found 210.1128.



2-Methyl-2-(3-nitro-2-phenylpropyl)-1,3-dioxolane was prepared in two steps from literature procedures, starting with a proline catalyzed Michael reaction between acetone and trans-nitrostyrene,[160] followed by protection of the ketone as the ketyl[149] affording 4.26 g (85%) of clear oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.32-7.14 (m, 5H), 4.86 (dd, *J* = 6.04, 12.63 Hz, 1H), 4.50 (dd, *J* = 9.33, 12.08 Hz, 1H), 3.91 (m, 4H), 3.72 (m, 1H), 2.06 (dd, *J* = 6.04, 7.69 Hz, 2H), 1.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.8, 128.7, 128.2, 127.2, 108.9, 80.7, 64.6, 64.3, 42.0, 39.7, 24.2; IR (neat) 2984, 2889, 1552, 1381, 1219, 1142, 1043, 763, 702 cm^{-1}; HRMS (Methane Chem Ion) *m/z* calcd for $[C_{13}H_{17}NO_4 + H]^+$ 252.1236, found 252.1240

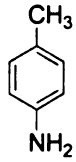
General Procedure D

General Procedure for the Reduction of Nitro Arenes to Amines: A round bottom flask was charged with palladium acetate (0.05 mmol, 11 mg), the nitroarene (1 mmol), and freshly distilled dry THF (5 mL). The flask was sealed and purged with nitrogen. While purging the flask with nitrogen a solution of aqueous KF was added via syringe (2 mmol KF, 116 mg; in 2 mL of degassed water). The nitrogen inlet was replaced with a balloon of nitrogen. PMHS (4 mmol, 0.24 mL; 1 mmol of hydride is 0.06mL) was slowly added dropwise via syringe (*Caution: Rapid addition PMHS can result in uncontrollable gas evolution!*) The reaction was stirred for 30 min or until complete as judged by TLC. At that time, the reaction flask was opened to the air, diluted with 5–10 mL of diethyl ether, and stirred for 5 minutes. The layers were separated and the aqueous layer was back extracted with diethyl ether. The combined organics were filtered through a plug of Celite (top layer) and neutral alumina (bottom layer) in a 1 cm diameter column by flushing with EtOAc. The filtrate was concentrated and subjected to flash chromatography using gradients of hexanes/EtOAc and/or EtOAc/MeOH.

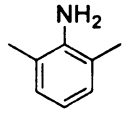


2-Aminotoluene: Subjection of 2-nitrotoluene (1 mmol, 0.117 mL) to the general procedure for reducing nitro arenes afforded 0.107 g (100%) of 2-aminotoluene as a yellow oil (silica gel FC, hexanes/EtOAc: 80/20 then 50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.06 (m, 2H), 6.79-6.62 (m, 2H), 3.60 (bs, 2H), 2.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.4, 130.3, 126.8, 122.2,

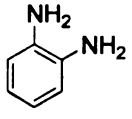
118.5, 114.8, 17.2. Physical and spectral data were consistent with commercially available material.



4-Aminotoluene: Subjection of 4-nitrotoluene (1 mmol, 0.1371 g) to the general procedure for reducing nitro arenes afforded 0.101 g (94%) of 4-aminotoluene as a yellow-orange solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 40–44°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.97 (d, *J* = 8.24 Hz, 2H), 6.61 (d, *J* = 8.24 Hz, 2H), 3.52 (bs, 2H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.7, 129.6, 127.6, 115.2, 20.3. Physical and spectral data were consistent with commercially available material.

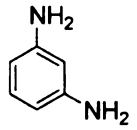


2-Amino-*m*-xylene: Subjection of 2-nitro-*m*-xylene (1 mmol, 0.136 mL) to the general procedure for reducing nitro arenes with 5 equivalents of PMHS (5 mmol, 0.3 mL) afforded 0.1211 g (100%) of 2-amino-*m*-xylene as a light yellow oil (silica gel FC, hexanes/EtOAc: 95/5 then 80/20). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.99 (d, *J* = 7.14 Hz, 2H), 6.70 (t, *J* = 7.69 Hz, 1H), 3.57 (bs, 2H), 2.23 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.7, 128.1, 121.5, 117.9, 17.5. Physical and spectral data were consistent with commercially available material.

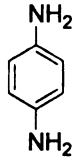


2-Aminoaniline: Subjection of 2-nitroaniline (1 mmol, 0.138 g) to the general procedure for reducing nitro arenes (full consumption of starting material as judged by TLC) followed by the addition of acetic anhydride (4 mmol, 0.376 mL) to the reaction mixture with an additional 30 minutes of stirring, afforded 0.1902 g (99%) of *N,N'*-(1,2-phenylene)diacetamide as a white

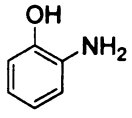
solid (silica gel FC, EtOAc/MeOH: 100/0 then 50/50); mp = 183–185°C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.31 (s, 2H), 7.53 (m, 2H), 7.10 (m, 2H), 2.05 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 168.6, 130.4, 124.7, 124.5, 23.6. Physical and spectral data were consistent with those previously reported.[150]



1,3-Benzenediamine: Subjection of 3-nitroaniline (1 mmol, 0.138 g) to the general procedure for reducing nitro arenes afforded 0.108 g (99%) of 1,3-benzenediamine as a green oil (silica gel FC, hexanes/EtOAc: 50/50 then 0/100). ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 6.56 (t, J = 7.69 Hz, 1H), 5.74 (dd, J = 2.19, 8.24 Hz, 2H), 5.69 (t, J = 2.19, 1H), 3.61 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 147.1, 129.0, 104.5, 100.8. Physical and spectral data were consistent with commercially available material.



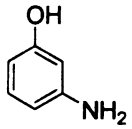
1,4-Benzenediamine: Subjection of 4-nitroaniline (1 mmol, 0.138 g) to the general procedure for reducing nitro arenes afforded 0.1033 g (95%) of 1,4-benzenediamine as a purple solid (silica gel FC, hexanes/EtOAc: 50/50 then 0/100); mp = 141°C. ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 6.32 (s, 4H), 3.28 (bs, 4H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 138.1, 116.0. Physical and spectral data were consistent with commercially available material.



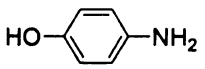
2-Aminophenol: Subjection of 2-nitrophenol (1 mmol, 0.139 g) to the general procedure for reducing nitro arenes afforded 0.1025 g (94%) of 2-aminophenol and 0.0052 g (4%) of the oxidized product as a red-yellow solid (silica gel FC, hexanes/EtOAc: 50/50). For 2-aminophenol: ^{1}H NMR

(300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.38 (bs, 1H), 6.56–6.25 (m, 4H), 3.62 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 144.0, 134.8, 119.4, 117.7, 114.9, 114.4.

Analytically pure material was obtained by following the general procedure for reducing nitro arenes with the following modification. After complete consumption of the starting material (as judged by TLC) acetic anhydride (2 mmol, 0.188 mL) was added to the reaction mixture followed by an additional 30 minutes of stirring to afford after the general workup 0.1481 g (98%) of 2-acetamidophenol as a white solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50 then 0/100); mp = 205 °C. ^1H NMR (300 MHz, DMSO-d_6): δ 9.70 (s, 1H), 9.29 (s, 1H), 7.64 (d, J = 7.69 Hz, 2H), 6.90–6.70 (m, 3H), 2.05 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 169.1, 147.9, 126.4, 124.7, 122.4, 119.0, 115.9, 23.6. Physical and spectral data were consistent with commercially available material.

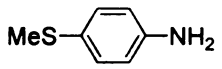


3-Aminophenol: Subjection of 3-nitrophenol (1 mmol, 0.139 g) to the general procedure for reducing nitro arenes afforded 0.1031 g (94%) of 3-aminophenol as a tan solid (silica gel FC, hexanes/EtOAc: 50/50); mp = 119–120 °C. ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.31 (bs, 1H), 6.60 (t, J = 8.24 Hz, 1H), 5.84 (dt, J = 1.64, 9.89 Hz, 3H), 3.62 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 157.4, 147.6, 129.2, 105.7, 104.5, 101.4. Physical and spectral data were consistent with commercially available material.

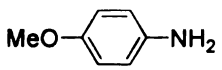


4-Aminophenol: Subjection of 4-nitrophenol (1 mmol, 0.139 g) to the general procedure for reducing nitro arenes afforded 0.0994 g (91%) of 4-

aminophenol and 0.008 g (7%) of the oxidized product as a tan solid (silica gel FC, hexanes/EtOAc: 50/50). For 4-aminophenol: ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 6.28 (d, J = 8.24 Hz, 2H), 6.19 (d, J = 8.24 Hz, 2H), 3.00 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 148.85, 138.41, 115.58, 115.22. Analytically pure material was obtained by following the general procedure for reducing nitro arenes with the following modification. After complete consumption of the starting material (as judged by TLC) acetic anhydride (2 mmol, 0.188 mL) was added to the reaction mixture followed by an additional 30 minutes of stirring to afford after the general workup 0.1496 g (99%) of acetaminophen as an off white solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50 then 0/100); mp = 166–168 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.61 (s, 1H), 9.11 (s, 1H), 7.31 (d, J = Hz, 2H), 6.64 (d, J = Hz, 2H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 167.7, 153.2, 131.1, 121.0, 115.1, 23.8. Physical and spectral data were consistent with commercially available material.



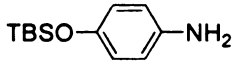
4-(Methylthio)aniline: Subjection of 4-nitrothioanisole (1 mmol, 0.169 g) to the general procedure for reducing nitro arenes afforded 0.150 g of a brown solid consisting of complex mixture of compounds of which ~10% was 4-(methylthio)aniline.



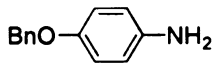
4-Methoxyaniline: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to the general procedure for reducing nitro arenes afforded 0.1209 g (98%) of 4-methoxyaniline as a tan solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 55–56°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.73 (d, J = 8.79 Hz,

2H), 6.61 (d, J = 8.79 Hz, 2H), 3.71 (s, 3H), 3.40 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.5, 139.8, 116.2, 114.6, 55.6. Physical and spectral data were consistent with commercially available material.

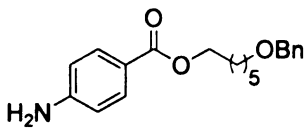
4-Acetoxyaniline: Subjection of 4-acetoxynitrobenzene[151] (1 mmol, 0.181 g) to the general procedure for reducing nitro arenes afforded 0.1427 g (94%) of 4-acetoxyaniline as a tan-red solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50, then 0/100); mp = 73 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 6.82 (d, J = 8.79 Hz, 2H), 6.59 (d, J = 8.79 Hz, 2H), 3.62 (bs, 2H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ170.0, 144.2, 142.4, 121.9, 115.3, 20.8. Physical and spectral data were consistent with those previously reported.[152]



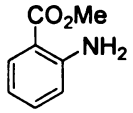
4-*tert*-Butyldimethylsiloxyaniline: Subjection of *tert*-Butyldimethyl-(4-nitro-phenoxy)-silane[153] (1 mmol, 0.253 g) to the general procedure for reducing nitro arenes with 3 equiv of PMHS (3 mmol, 0.18 mL) afforded 0.2054 g (92%) of 4-*tert*-butyldimethylsiloxyaniline as a dark yellow oil and 0.0075 g (7%) of 4-aminophenol (silica gel FC, hexanes/EtOAc: 80/20, 50/50, then 0/100). For 4-*tert*-butyldimethylsiloxyaniline: ^1H NMR (300 MHz, $CDCl_3$): δ 6.65 (d, J = 8.79 Hz, 2H), 6.56 (d, J = 8.79 Hz, 2H), 3.91 (bs, 2H), 0.94 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.7, 126.0, 120.6, 116.5, 115.5, 18.1, –4.5. IR (neat) 3460, 2957, 2930, 2858, 1591, 1510, 1336, 1248, 912, 841, 781 cm^{-1}; LRMS (EI, 70 eV) 224 (11), 223 (93), 167 (29), 166 (100), 138 (38), 109 (12), 93 (7), 73 (17), 65 (34); HRMS (EI) *m/z* calcd for $C_{12}H_{21}NOSi$ 223.1392, found 223.1398.



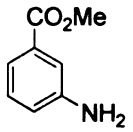
4-(Benzyloxy)aniline: Subjection of 1-(benzyloxy)-4-nitrobenzene (1 mmol, 0.229 g) to the general procedure for reducing nitro arenes afforded 0.0549 g (28%) of 4-(benzyloxy)aniline as red-orange solid, along with 0.0784 g (56%) of 4-nitrophenol and 0.0156g (14%) 4-aminophenol (silica gel FC, hexanes/EtOAc: 80/20, 50/50, then 0/100); mp = 56 °C. For 4-(benzyloxy)aniline: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (m, 5H), 6.80 (d, *J* = 8.69 Hz, 2H), 6.62 (d, *J* = 8.79 Hz, 2H), 4.97 (s, 2H), 3.43 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.9, 140.1, 137.4, 128.4, 127.7, 127.4, 116.3, 116.0, 70.7; spectral data were consistent with those previously reported.[154]



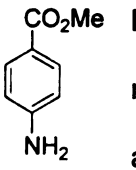
6-(Benzyloxy)hexyl 4-aminobenzoate: Subjection of 6-(benzyloxy)hexyl 4-nitrobenzoate (1 mmol, 0.357 g) to the general procedure for reducing nitro arenes afforded 0.3272 g (100%) of 6-(benzyloxy)hexyl 4-aminobenzoate as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 58-59 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.79 Hz, 2H), 7.31 (m, 5H), 6.59 (d, *J* = 8.79 Hz, 2H), 4.48 (s, 2H), 4.22 (t, *J* = 6.59 Hz, 2H), 4.03 (bs, 2H), 3.45 (t, *J* = 6.59 Hz, 2H), 1.71 (t, *J* = 6.59 Hz, 2H), 1.64 (t, *J* = 6.59 Hz, 2H), 1.41 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 150.7, 138.5, 131.5, 128.3, 127.5, 127.4, 119.9, 113.7, 72.8, 70.2, 64.3, 29.6, 28.7, 25.9, 25.8; IR (PTFE card, neat) 3470, 3366, 3235, 2936, 2858, 1689, 1603, 1309, 1275, 1170, 1109, 843, 771, 736, 698 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{20}H_{25}NO_3$ 327.1834, found 327.1832.



Methyl 2-aminobenzoate: Subjection of methyl 2-nitrobenzoate (1 mmol, 0181 g) to the general procedure for reducing nitro arenes afforded 0.1511 g (100%) of methyl 2-aminobenzoate as a bright yellow oil (silica gel FC, hexanes/EtOAc: 80/20). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 1.64 and 8.24 Hz, 1H), 7.23 (dt, *J* = 1.64 and 7.14 Hz, 1H), 6.61 (m, 2H), 5.69 (bs, 2H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.5, 150.3, 133.9, 131.2, 116.5, 116.1, 110.5, 51.3. Physical and spectral data were consistent with commercially available material.

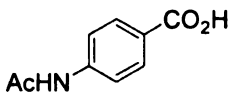


Methyl 3-aminobenzoate: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to the general procedure for reducing nitro arenes afforded 0.1511 g (100%) of methyl 3-aminobenzoate as a light yellow oil (silica gel FC, hexanes/EtOAc: 80/20 then 50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (d, *J* = 7.69 Hz, 1H), 7.29 (m, 1H), 7.13 (t, 7.69 Hz, 1H), 6.78 (m, 1H), 3.85 (bs, 2H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 146.5, 130.8, 129.0, 125.2, 119.2, 115.5, 51.8. Physical and spectral data were consistent with commercially available material.

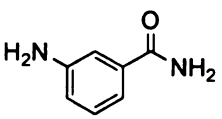


Methyl 4-aminobenzoate: Subjection of methyl 4-nitrobenzoate (1 mmol, 0.181 g) to the general procedure for reducing nitro arenes afforded 0.1511 g (100%) of methyl 4-aminobenzoate as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.24 Hz, 2H), 6.57 (d, *J* = 8.79 Hz, 2H), 4.13 (bs, 2H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 150.9, 131.4, 119.1,

113.5, 51.4. Physical and spectral data were consistent with commercially available material.

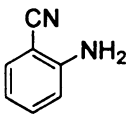


4-Acetylaminobenzoic acid: 4-Nitrobenzoic acid (1 mmol, 0.167 g) was subjected to the general procedure for reducing nitro arenes with the following modification. After complete consumption of the starting material (as judged by TLC) acetic anhydride (2 mmol, 0.188 mL) was added to the reaction mixture followed by an additional 30 minutes of stirring. Following the general extraction protocol, the organics were filtered though a plug of Celite. Concentration of the crude material and flash chromatography afforded 0.1689 g (94%) of 4-acetylaminobenzoic acid as a white solid (silica gel FC, hexanes/EtOAc: 50/50, 0/100, then 80/20[EtOAc/MeOH]); mp = 259–262 °C. ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 9.98 (s, 1H), 7.90 (d, J = 8.24 Hz, 2H), 7.68 (d, J = 8.24 Hz, 2H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 168.7, 167.2, 142.9, 130.1, 124.9, 118.1, 23.9. Physical and spectral data were consistent with commercially available material.



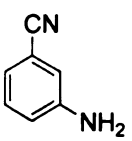
3-Aminobenzamide: Subjection of 3-nitrobenzamide (1 mmol, 0.166 g) to the general procedure for reducing nitro arenes afforded 0.125 g (92%) of 3-aminobenzamide as a white solid (silica gel FC, EtOAc/MeOH: 100/0 then 80/20); mp = 117–117.5°C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.69 (bs, 1H), 7.11 (bs, 1H), 7.05–6.86 (m, 3H), 6.62 (d, J = 7.69 Hz, 1H), 5.14 (bs 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 168.2, 148.6, 135.1,

128.6, 116.5, 114.7, 113.1. Physical and spectral data were consistent with commercially available material.



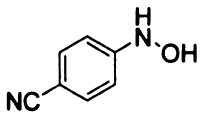
2-Aminobenzonitrile: Subjection of 2-nitrobenzonitrile (1 mmol, 0.148 g) to the general procedure for reducing nitro arenes with stirring for 12 h afforded 0.1147 g (97%) of 2-aminobenzonitrile as a tan solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 52 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.22 (m, 2H), 6.69 (m, 2H), 4.42 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.6, 133.9, 132.2, 117.7, 115.0, 95.7. Physical and spectral data were consistent with commercially available material.

Subjection of 2-nitrobenzonitrile (1 mmol, 0.148 g) to the general procedure for reducing nitro arenes with 4 equiv KF (4 mmol, 0. 232 g) and stirring for 4 h afforded 0.1150 g (97%) of 2-aminobenzonitrile.

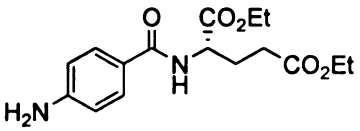


3-Aminobenzonitrile: Subjection of 3-nitrobenzonitrile (1 mmol, 0.148 g) to the general procedure for reducing nitro arenes with stirring for 12 h afforded 0.1155 g (98%) of 3-aminobenzonitrile as a yellow-orange solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 49–50 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16 (t, J = 7.96, 1H), 6.94 (m, 1H), 6.88–6.78 (m, 2H), 3.85 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.9, 129.8, 121.6, 119.1, 119.1, 117.2, 112.5. Physical and spectral data were consistent with commercially available material.

Subjection of 3-nitrobenzonitrile (1 mmol, 0.148 g) to the general procedure for reducing nitro arenes with 4 equiv KF (4 mmol, 0. 232 g) and stirring for 4 h afforded 0.1151 g (97%) of 3-aminobenzonitrile.

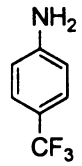


4-Aminobenzonitrile: Subjection of 4-nitrobenzonitrile (1 mmol, 0.148 g) to the general procedure for reducing nitro arenes with stirring for 12 h afforded an inseparable mixture of 0.1043 g (78%) of 4-hydroxyaminobenzonitrile and 0.0094 g (8%) of 4-aminobenzonitrile as a bright yellow solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50). For 4-hydroxyaminobenzonitrile: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.37 (d, *J* = 8.79 Hz, 2H), 7.29 (bs, 1H), 6.87 (d, *J* = 8.24 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.5, 133.5, 132.9, 119.7, 114.1, 112.8, 102.1. Physical and spectral data were consistent with those previously reported.[155]

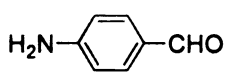


(*S*)-Diethyl 2-(4-aminobenzamido)pentanedioate : Subjection of *N*-(4-nitrobenzoyl)-L-glutamic acid diethyl ester (1 mmol, 0.352 g) to the general procedure for reducing nitro arenes afforded 0.3222 g (100%) of (*S*)-Diethyl 2-(4-aminobenzamido)pentanedioate as white solid (silica gel FC, hexanes/EtOAc: 0/100); mp = 134-136 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (d, *J* = 8.24 Hz, 2H), 6.80 (d, *J* = 7.14 Hz, 1H), 6.57 (d, *J* = 8.79 Hz, 2H), 4.71 (dt, *J* = 4.94 and 8.24 Hz, 1H), 4.15 (q, *J* = 7.14 Hz, 2H), 4.03 (q, *J* = 7.14 Hz, 2H), 4.2-3.9 (bs, 2H), 2.38 (m, 2H), 2.23 (m, 1H), 2.05 (quin, *J* = 7.14 Hz, 1H), 1.22 (t, *J* = 7.14 Hz, 3H), 1.14 (t, *J* = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.1, 172.2, 166.8, 149.9, 128.8, 122.8, 113.9, 61.5, 60.6, 52.0,

30.4, 27.3, 14.0; IR (PTFE card, neat) 3445, 3314, 2974, 1726, 1638, 1606, 1529, 1504, 1298, 1182, 1103, 1022 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{16}H_{22}N_2O_5$ 322.1529, found 322.1527.

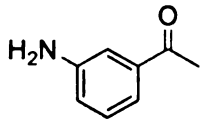


1-Amino-4-(trifluoromethyl)benzene: Subjection of 4-nitrotrifluorotoluene (1 mmol, 0.191 g) to the general procedure for reducing nitro arenes afforded 0.1610 g (99%, 90% purity, contaminated with siloxane) of 1-amino-4-(trifluoromethyl)benzene as a yellow oil (silica gel FC, hexanes/EtOAc: 80/20 then 50/50). Pure product could be obtained by following the general procedure for reducing nitro arenes with the following modification. After filtration through the plug of Celite/alumina the filtrate was stirred with 5 mol% TBAF for 4 hours. The reaction was concentrated and subjecting to flash chromatography to afford 1-amino-4-(trifluoromethyl)benzene that was contaminated with TBA and traces of siloxane (quantitative yield, 95% purity). Short-path distallation of this crude material afforded 1-amino-4-(trifluoromethyl)benzene (91%); b.p. = 75 °C at 1 mm Hg. ^1H NMR (300 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8.24 Hz, 2H), 6.65 (d, *J* = 8.24 Hz, 2H), 3.91 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.4, 126.67, 126.62, 126.56, 126.52, 123.0, 120.1, 119.7, 114.1, 107.9. Physical and spectral data were consistent with commercially available material.



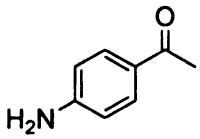
4-Aminobenzaldehyde: Subjection of 4-nitrobenzaldehyde (1 mmol, 0.151 g) to the general procedure for reducing nitro arenes with afforded an inseparable mixture of 0.0879 g (73%) of 4-aminobenzaldehyde and 0.0376 g

(24%) of (4-nitrophenyl)-methanol as a yellow solid containing residual ethyl acetate (silica gel FC, hexanes/EtOAc: 50/50). Upon complete removal of the ethyl acetate a yellow solid formed, which was insoluble in all solvents tested (presumable from polymerization of the two products). For 4-aminobenzaldehyde: ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.62 (s, 1H), 7.58 (d, *J* = 6.59 Hz, 2H), 6.62 (d, *J* = 6.59 Hz, 2H), 4.55 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.6, 152.8, 132.3, 126.9, 113.8; For (4-nitrophenyl)-methanol: ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (d, *J* = 6.59 Hz, 2H), 7.46 (d, *J* = 7.14 Hz, 2H), 4.73 (s, 2H), 3.70 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.6, 126.8, 123.4, 63.6

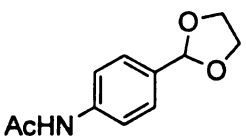


3'-Aminoacetophenone: Subjection of 3-nitroacetophenone (1 mmol, 0.165 g) to the general procedure for reducing nitro arenes with 3 equiv of PMHS (3 mmol, 0.18 mL) afforded 0.1208 g (89%) of 3'-aminoacetophenone as a cream yellow solid (silica gel FC, hexanes/EtOAc: 50/50); mp = 94–95°C and 0.0122g (7%) of starting material. For 3'-aminoacetophenone: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29–7.12 (m, 3H), 6.80 (dd, *J* = 2.19 and 7.69 Hz, 1H), 3.86 (bs, 2H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.4, 146.7, 137.9, 129.2, 119.5, 118.5, 113.8, 26.5. Physical and spectral data were consistent with commercially available material.

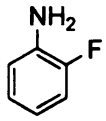
Subjection of 3-nitroacetophenone (1 mmol, 0.165 g) to the general procedure for reducing nitro arenes with 3.5 equiv of PMHS (3.5 mmol, 0.21 mL) afforded 0.1316 g (97%) of 3'-aminoacetophenone.



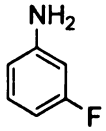
4'-Aminoacetophenone: Subjection of 4-nitroacetophenone (1 mmol, 0.165 g) to the general procedure for reducing nitro arenes with 3 equiv of PMHS (3 mmol, 0.18 mL) afforded 0.1291 g (95%) of 4'-aminoacetophenone as a yellow solid; mp = 102°C, and 0.0064 g (4%) of starting material (silica gel FC, hexanes/EtOAc: 80/20 then 50/50). For 4'-aminoacetophenone: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (d, *J* = 6.59 Hz, 2H), 6.69 (d, *J* = 6.59 Hz, 2H), 4.47 (bs, 2H), 2.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.4, 151.0, 130.7, 127.7, 113.6, 26.0. Physical and spectral data were consistent with commercially available material.



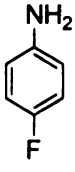
***N*-(4-(1,3-Dioxolan-2-yl)phenyl)acetamide**: Subjection of 2-(4-nitrophenyl)-1,3-dioxolane (1 mmol, 0.195 g) to the general procedure for reducing nitro arenes with the following modification. After complete consumption of the starting material (as judged by TLC) acetic anhydride (2 mmol, 0.188 mL) was added to the reaction mixture followed by an additional 30 minutes of stirring, affording 0.1649 g (80%) of *N*-(4-(1,3-Dioxolan-2-yl)phenyl)acetamide as light yellow solid (silica gel FC, hexanes/EtOAc: 50/50 then 0/100); mp = 110 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.60 (bs, 1H), 7.45 (d, *J* = 8.79 Hz, 2H), 7.32 (d, *J* = 8.79 Hz, 2H), 5.68 (s, 1H), 3.98 (m, 4H), 2.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 138.8, 133.2, 126.9, 119.6, 103.2, 64.9, 24.0; IR (PTFE card, neat) 3310, 3127, 3063, 2885, 1670, 1604, 1539, 1419, 1371, 1313, 1078, 941, 835 cm^{-1}; LRMS (EI, 70eV) 207 (0.36), 163 (41), 121 (85), 120 (83), 119 (100), 92 (45), 77 (4), 73 (3), 43 (83); HRMS (Chem ion) *m/z* calcd for $[C_{11}H_{13}NO_3 + H]^+$ 208.0974, found 208.0970



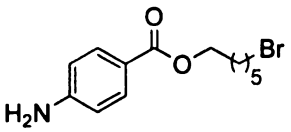
2-Fluoroaniline: Subjection of 1-fluoro-2-nitrobenzene (1 mmol, 0.105 mL) to the general procedure for reducing nitro arenes afforded 0.1087 g (97%) of 2-fluoroaniline as a light yellow oil (silica gel FC, hexanes/EtOAc: 80/20). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.00–6.86 (m, 2H), 6.78–6.18 (m, 2H), 3.67 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.2, 150.0, 134.5, 124.4, 124.3, 118.5, 118.4, 116.8, 115.2. Physical and spectral data were consistent with commercially available material.



3-Fluoroaniline: Subjection of 1-fluoro-4-nitrobenzene (1 mmol, 0.106 mL) to the general procedure for reducing nitro arenes afforded 0.1069 g (96%) of 3-fluoroaniline as a light yellow oil (silica gel FC, hexanes/EtOAc: 80/20, then 50/50); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.03 (q, J = 8.24 Hz, 1H), 6.45–6.28 (m, 3H), 3.74 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.3, 162.1, 148.3, 148.1, 130.3, 130.2, 110.5, 104.9, 104.6, 101.9, 101.6. Physical and spectral data were consistent with commercially available material.

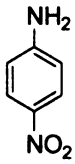


4-Fluoroaniline: Subjection of 1-fluoro-4-nitrobenzene (1 mmol, 0.106 mL) to the general procedure for reducing nitro arenes afforded 0.1051 g (95%) of 4-fluoroaniline as a light yellow oil (silica gel FC, hexanes/EtOAc: 80/20 then 50/50). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.83 (m, 2H), 6.60 (m, 2H), 3.51 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.9, 154.7, 142.3, 116.0, 115.9, 115.7, 115.4. Physical and spectral data were consistent with commercially available material.

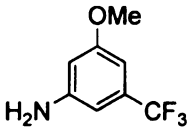


6-Bromohexyl 4-aminobenzoate: Subjection of 6-bromohexyl 4-nitrobenzoate (1 mmol, 0.333 g) to the general procedure for reducing nitro arenes with 3.5 equiv. PMHS (3.5 mmol, 0.21 mL) afforded 0.3002 g (100%) of 6-bromohexyl 4-aminobenzoate as a white solid (silica gel FC, hexanes/EtOAc: 95/5 then 50/50); mp = 77–78 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.79 Hz, 2H), 6.58 (d, *J* = 8.79 Hz, 2H), 4.21 (t, *J* = 6.59 Hz, 2H), 4.07 (bs, 2H), 3.35 (t, *J* = 6.59 Hz, 2H), 1.82 (quin, *J* = 6.59 Hz, 2H), 1.69 (quin, *J* = 6.59 Hz, 2H), 1.42 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 150.8, 131.3, 119.4, 113.5, 64.1, 33.7, 32.4, 28.4, 27.6, 25.1; IR (THF solution) 3445, 3360, 3238, 2937, 1705, 1604, 1518, 1275, 1170, 1113, 844, 773 cm^{-1}; LRMS (EI, 70 eV) 300 (12), 299 (11), 138 (12), 137 (100), 80 (7), 79 (100), 92 (40), 65 (15), 64 (14); HRMS (EI) *m/z* calcd for $C_{13}H_{18}BrNO_2$ 299.0521, found 299.0525.

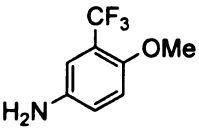
Subjection of 6-bromohexyl 4-nitrobenzoate (1 mmol, 0.333 g) to the general procedure for reducing nitro arenes afforded 0.2453 g (82%) of 6-bromohexyl 4-aminobenzoate, and 0.0332 g (15%) of hexyl 4-aminobenzoate; for hexyl 4-aminobenzoate: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.24 Hz, 2H), 6.59 (d, *J* = 8.24 Hz, 2H), 4.21 (t, *J* = 6.59 Hz, 2H), 3.99 (bs, 2H), 1.70 (m, 2H), 1.30 (m, 6H), 0.87 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 150.6, 131.4, 120.0, 113.7, 64.5, 31.4, 28.7, 25.7, 22.5, 13.9.



4-Nitroaniline: Subjection of 1,4-dinitrobenzene (1 mmol, 0.168 g) to the general procedure for reducing nitro arenes afforded 0.0994 g (72%) of 4-nitroaniline as an orange solid, mp = 147–148°C and 0.0217g (20%) of 1,4-diaminobenzene as a tan solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50, 0/100, then 80/20[EtOAc/MeOH]). For 4-nitroaniline: ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 7.68 (d, J = 8.79 Hz, 2H), 6.32 (d, J = 9.34 Hz, 2H), 5.27 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 153.7, 136.7, 125.6, 112.2. Physical and spectral data were consistent with commercially available material.

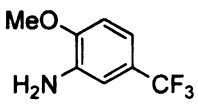


3-Methoxy-5-(trifluoromethyl)aniline: Subjection of 3-methoxy-5-nitro-benzotrifluoride (1 mmol, 0.221 g) to the general procedure for reducing nitro arenes was done with 5 equiv of PMHS (5 mmol, 0.3 mL) and stirred for 12 hours, affording 0.19g (99%) of 3-methoxy-5-(trifluoromethylaniline as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 50 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.51 (s, 1H), 6.48 (s, 1H), 6.31 (s, 1H), 3.92 (bs, 2H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.9, 148.0, 132.6, 132.2, 125.8, 122.2, 104.45, 104.40, 103.6, 100.7, 55.2. Physical and spectral data were consistent with commercially available material.

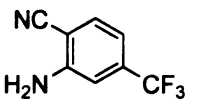


4-Methoxy-3-(trifluoromethyl)aniline: Subjection of 2-methoxy-5-nitro-benzotrifluoride (1 mmol, 0.221 g) to the general procedure for reducing nitro arenes afforded 0.1883 g (98.5%) of 4-methoxy-3-(trifluoromethyl)aniline as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 55-57 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ

6.87 (d, J = 2.74 Hz, 1H), 6.80 (m, 1H), 6.76 (dd, J = 2.74, 8.79 Hz, 1H), 3.78 (s, 3H), 3.53, (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.9, 139.3, 125.1, 121.1, 119.0, 118.8, 113.7, 113.6, 113.56, 113.50, 56.2; IR (Nujol) 3431, 3314, 3211, 1643, 1599, 1508, 1437, 1344, 1236, 1101, 1053, 1022, 877, 815, 709 cm^{-1}; LRMS (EI, 70eV) 192 (8), 191 (78), 177 (12), 176 (100), 175 (10), 148 (42), 129 (13), 128 (30), 101 (30), 98 (21), 77 (10), 51 (25); HRMS (EI) *m/z* calcd for $C_8H_8F_3NO$ 191.0558, found 191.0555

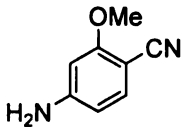


2-Methoxy-5-(trifluoromethyl)aniline: Subjection of 4-methoxy-3-nitro-benzotrifluoride (1 mmol, 0.221 g) to the general procedure for reducing nitro arenes afforded 0.1911 g (100%) of 2-methoxy-5-(trifluoromethyl)aniline as a white solid (silica gel FC, hexanes/EtOAc: 80/20); mp = 56-57 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 6.96 (d, J = 8.24 Hz, 1H), 6.89 (s, 1H), 6.77 (d, J = 8.24 Hz, 1H), 3.90 (bs, 2H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.3, 136.4, 126.3, 123.3, 122.7, 115.49, 115.43, 111.0, 110.9, 109.5, 55.4.

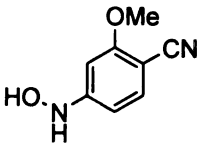


2-Amino-4-(trifluoromethyl)benzonitrile: Subjection of 2-nitro-4-(trifluoromethyl)benzonitrile (1 mmol, 0.216 g) to the general procedure for reducing nitro arenes afforded 0.1451g (78%) of 2-amino-4-(trifluoromethyl)benzonitrile as a yellow solid, and 0.0411g (20%) of 2-amino-4-(trifluoromethyl)benzamide (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 85 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.44 (d, J = 8.24 Hz, 1H), 6.95 (s, 1H),

6.90 (d, J = 8.24 Hz, 1H), 4.71 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.7, 135.8, 135.4, 133.1, 124.9, 121.2, 116.3, 114.04, 114.00, 111.86, 111.80, 98.6.

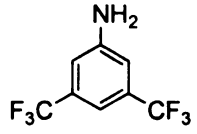


4-Amino-2-methoxybenzonitrile: Subjection of 2-methoxy-4-nitrobenzonitrile (1 mmol, 0.178 g) to the general procedure for reduction of nitro arenes with stirring for 1 hour afforded 0.1473 g (99%) of 4-amino-2-methoxybenzonitrile as a burgundy solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 94 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.21 (d, J = 8.24 Hz, 1H), 6.18 (dd, J = 2.19, 8.24 Hz, 1H), 6.13 (m, 1H), 4.26 (bs, 2H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.9, 152.4, 134.7, 117.9, 106.9, 96.7, 89.6, 55.6; IR (PTFE card, neat) 1603, 1512, 1471, 1342, 1130, 1028, 833, 636 cm^{-1}; LRMS (EI, 70eV) 148 (100), 119 (36), 118 (29), 105 (28), 104 (28), 91 (23), 78 (25), 77 (10); HRMS (EI) *m/z* calcd for $C_8H_8N_2O$ 148.0637, found 148.0633.

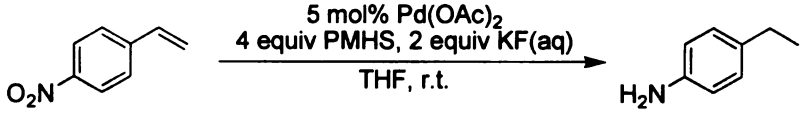


Subjection of 2-methoxy-4-nitrobenzonitrile (1 mmol, 0.178 g) to the general procedure for reduction of nitro arenes with stirring for 30 minutes afforded 0.1631 g (99%) of 4-(hydroxyamino)-2-methoxybenzonitrile as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); ^1H NMR (300 MHz, $CDCl_3$): δ 7.19 (d, J = 8.79 Hz, 1H), 6.20 (d, J = 1.64 Hz, 1H), 6.15 (dd, J = 2.19, 8.24 Hz, 1H), 6.12 (bs, 2H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.4, 154.8, 134.2, 118.3, 106.4, 95.6, 85.5, 55.3.

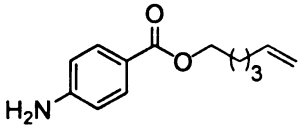
4-Aminophthalonitrile: Subjection of 4-nitrophthalonitrile (1 mmol, 0.173 g) to the general procedure for reduction of nitro arenes afforded a complex mixture of material. All starting material was consumed.



3,5-Bis(trifluoromethyl)aniline: Subjection of 3,5-bis(trifluoromethyl)nitrobenzene (1 mmol, 0.169 mL) to the general procedure for reduction of nitro arenes afforded an inseparable mixture of the amine and *N*-hydroxylamine in a ratio that varied for each run. For 3,5-bis(trifluoromethyl)aniline: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18 (s, 1 H), 7.00 (s, 2H); for *N*-(3,5-bis(trifluoromethyl)phenyl)hydroxylamine: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (s, 1H), 7.32 (s, 2H) 5.60 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.0, 147.2, 132.5, 132.3, 132.1, 131.7, 128.7, 125.1, 121.4, 117.8, 115.2, 114.3, 113.7, 111.7.



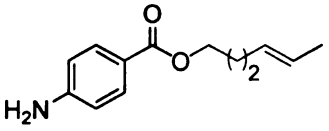
4-Ethylaniline: Subjection of 4-nitrostyrene (1 mmol, 0.149 g) to the general procedure for reduction nitro arenes afforded 0.1200 g (99%) of 4-ethylaniline as yellow oil (silica gel FC; hexanes/EtOAc: 80/20 then 50/50); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.97 (d, *J* = 8.29 Hz, 2H), 6.61 (d, *J* = 8.29 Hz, 2H), 3.47 (bs, 2H), 2.52 (q, *J* = 7.69 Hz, 2H), 1.16 (t, *J* = 7.69 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.9, 134.4, 128.5, 115.2, 27.9, 15.9.



Hex-5-enyl 4-aminobenzoate: Subjection of hex-5-enyl 4-nitrobenzoate (1 mmol, 0.249 g) to the general

procedure for reducing nitro arenes afforded 0.2205 g of hex-5-enyl 4-aminobenzoate (27%) and hexyl 4-aminobenzoate (73%) as an inseparable mixture in a 1 to 2.68 ratio, as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.79 Hz, 2H), 6.59 (d, *J* = 8.79 Hz, 2H), 5.42 (m, 3H, measured 0.81 H), 4.21 (t, *J* = 6.59 Hz, 2H), 4.05 (bs, 2H), 2.08 (m, 2H, measured 0.54H), 1.83-1.53 (m, 3H), 1.45-1.20 (m, 3.5H), 0.87 (t, *J* = 6.59 Hz, 3H, measured 2.15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 150.8, 131.4, 130.0, 125.6, 119.7, 113.6, 64.4, 63.7, 31.3, 28.9, 28.6, 28.5, 25.6, 22.4, 17.7, 13.9.

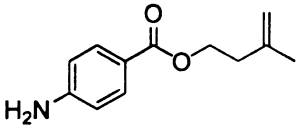
Subjection of hex-5-enyl 4-nitrobenzoate to the general procedure for reducing nitro arenes with 3 equiv of PMHS (3 mmol, 0.18 mL) afforded 0.1633 g of hex-5-enyl 4-aminobenzoate (19%) and hexyl 4-aminobenzoate (55%) as an inseparable mixture in a 1 to 2.89 ratio, and 0.692 g of the nitro arene in a 1 to 1 ratio of olefin to aliphatic.



(E)-Hex-4-enyl 4-aminobenzoate: Subjection of (E)-hex-4-enyl 4-nitrobenzoate (1 mmol, 0.249 g) to the general procedure for reducing nitro arenes with 3 equivalents of PMHS (3 mmol, 0.18 mL), afforded 0.1608 g of (E)-hex-4-enyl 4-aminobenzoate (51%) and hexyl 4-aminobenzoate (22%) as an inseparable mixture in a 2.25 to 1 ratio, as a tan solid (silica gel FC, hexanes/EtOAc: 80/20); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.79 Hz, 2H), 6.58 (d, *J* = 8.79 Hz, 2H), 5.41 (m, 2H, measured 1.38H), 4.21 (t, *J* = 6.59 Hz, 2H), 4.11 (bs, 2H), 2.07 (m, 2H, measured 1.38H), 1.75 (m,

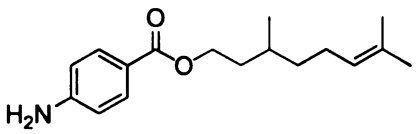
2H), 1.61 (m, 3H, measured 2.08H), 1.31 (m, 6H, measured 1.84H), 0.86 (t, J = 6.59 Hz, 3H, measured 0.92H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 166.6, 150.9, 150.8, 131.3, 129.5, 125.5, 119.5, 119.4, 113.5, 64.3, 63.7, 31.3, 28.8, 28.6, 28.4, 25.5, 22.3, 17.7, 13.8. 0.0673 g of nitroarene was also isolated in 2.77/1 ratio of S.M. to aliphatic.

Subjection of (E)-hex-4-enyl 4-nitrobenzoate (1 mmol, 0.249 g) to the general procedure for reducing nitro arenes afforded 0.2098 g of (E)-hex-4-enyl 4-aminobenzoate (41%) and hexyl 4-aminobenzoate (54%) as an inseparable mixture in a 1/1.325 ratio.

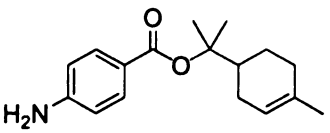


3-Methylbut-3-enyl 4-aminobenzoate: Subjection of 3-methylbut-3-enyl 4-nitrobenzoate (1 mmol 0.235 g) to the general procedure for reducing nitroarenes with 3.5 equivalents of PMHS (3.5 mmol, 0.21 mL), afforded 0.2007 g of 3-methylbut-3-enyl 4-aminobenzoate (64%), 3-methylbut-2-enyl 4-aminobenzoate (18%), and isopentyl 4-aminobenzoate (15%) as an inseparable mixture in a 4.12/1.15/1 ratio, as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20); ^1H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, J = 8.24 Hz, 2H), 6.57 (d, J = 8.24 Hz, 2H), 5.41 (m, 1H, measured 0.19H), 4.77 (d, J = 7.69 Hz, 2H, measured 1.36H), 4.72 (d, J = 7.14 Hz, 2H, measured 0.36H), 4.33 (t, J = 7.14 Hz, 2H, measured 1.31H), 4.25 (t, J = 7.14 Hz, 2H, measured 0.37H), 4.11 (bs, 2H), 2.41 (t, J = 6.59 Hz, 2H, measured 1.31H), 1.75 (s, 3H, measured 1.97H), 1.70 (d, J = 7.69 Hz, 6H, measured 1.09H), 1.60 (q, J = 6.59 Hz, 2H, measured 0.32H), 0.91 (d, J = 6.59 Hz, 6H,

measured 0.96H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 150.9, 150.8, 141.8, 138.4, 131.4, 119.5, 118.9, 113.6, 112.1, 62.8, 62.5, 61.1, 37.3, 36.7, 25.6, 25.0, 22.43, 22.40, 17.9.



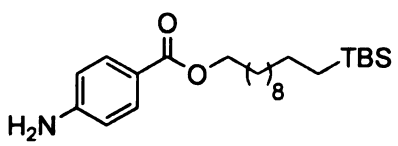
3,7-Dimethyloct-6-enyl 4-aminobenzoate: Subjection of 3,7-dimethyloxt-6-enyl 4-nitrobenzoate (1 mmol, 0.305 g) to the general procedure for reducing nitro arenes with 3.5 eq PMHS (3.5 mmol, 0.21 mL) afforded an inseparable mixture, 0.2491 g (90.5%) of 3,7-dimethyloct-6-enyl 4-aminobenzoate, and 0.0126 g (4.5%) of 3,7-dimethyloctyl 4-aminobenzoate as yellow oil (silica gel FC, hexanes/EtOAc: 80/20); ^1H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.79 Hz, 2H), 6.59 (d, *J* = 8.79 Hz, 2H), 5.06 (m, 1H), 4.26 (m, 2H), 4.09 (bs, 2H), 1.97 (m, 2H), 1.81 – 1.08 (m, 12H), 0.93 (d, J = 6.59 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 150.8, 131.4, 131.1, 124.5, 119.7, 113.6, 62.7, 36.8, 35.4, 29.4, 25.5, 25.2, 19.3, 17.5; IR (neat) 3478, 3372, 3231, 2961, 2926, 1893, 1624, 1604, 1278, 1172, 1115 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{17}H_{25}NO_2$ 275.1885, found 275.1883.



2-(4-Methylcyclohex-3-enyl)propan-2-yl 4-aminobenzoate: Subjection of 2-(4-methylcyclohex-3-enyl)propan-2-yl 4-nitrobenzoate (1 mmol, 0.303 g) to the general procedure for reducing nitro arenes with 3.5 eq PMHS (3.5 mmol, 0.21 mL) afforded an inseparable mixture, 0.2538 g (92.7%) of 2-(4-methylcyclohex-3-enyl)propan-2-yl 4-aminobenzoate, and 0.0197 g (7.1%) of 2-(4-methylcyclohexyl)propan-2-yl 4-

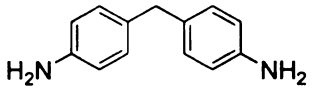
aminobenzoate as clear viscous oil (silica gel FC, hexanes/EtOAc: 80/20); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.79 Hz, 2H), 6.56 (d, *J* = 8.24 Hz, 2H), 5.35 (s, 1H), 4.07 (bs, 2H), 2.2-1.8 (m, 7H), 1.62 (s, 3H), 1.54 (s, 3H), 1.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.7, 150.5, 133.7, 131.1, 121.3, 120.3, 113.5, 84.3, 43.0, 30.8, 26.3, 23.8, 23.4, 23.1; IR (neat) 3478, 3370, 3229, 2928, 1684, 1616, 1516, 1437, 1311, 1172, 1115, 912, 844, 771, 734 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{17}H_{22}NO_2$ 273.1729, found 273.1736.

11-(*tert*-butyldimethylsilyl)undec-10-enyl 4-aminobenzoate: Subjection of 11-(tert-butyldimethylsilyl)undec-10-ynyl 4-nitrobenzoate (1 mmol, 0.431 g) to the general procedure for reduction of nitro arenes afforded 0.3899 g of (Z)-11-(tert-butyldimethylsilyl)undec-10-enyl 4-aminobenzoate, (E)-11-(tert-butyldimethylsilyl)undec-10-enyl 4-aminobenzoate, (E)-11-(tert-butyldimethylsilyl)undec-9-enyl 4-aminobenzoate, and 11-(tert-butyldimethylsilyl)undecyl 4-aminobenzoate as an inseparable mixture, in a 2.25/1.50/1.05/1 ratio, as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20).

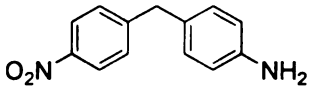


11-(*tert*-butyldimethylsilyl)undecyl 4-aminobenzoate: Subjection of 11-(tert-butyldimethylsilyl)undec-10-ynyl 4-nitrobenzoate (1mmol, 0.431 g) to the general procedure for reduction of nitro arenes with 6 equiv PMHS (6 mmol, 0.36 mL) afforded 0.3643 g (89%) of 11-(tert-butyldimethylsilyl)undecyl 4-aminobenzoate as a white solid (silica gel FC, hexanes/EtOAc: 90/10); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.79 Hz, 2 H), 6.60 (d, *J* = 8.79 Hz, 2H), 4.22 (t, *J* = 6.59

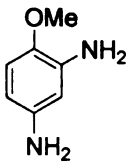
Hz, 2H), 4.02 (quin, J = 6.59 Hz, 2H), 1.24 (m, 18H), 0.83 (s, 9H), -0.11 (s, 6H, measured 5H);[13]C NMR (75 MHz, $CDCl_3$): δ 166.7, 150.6, 131.5, 120.1, 113.7, 64.5, 33.9, 29.6, 29.5, 29.3, 29.2, 28.7, 26.5, 26.0, 24.2, 16.5, 12.4, -6.3.



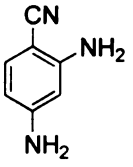
4,4'-Diaminodiphenylmethane: Subjection of bis(4-nitrophenyl)methane (1 mmol, 0.258 g) to the general procedure for reducing nitro arenes with 8 equiv of PMHS (8 mmol, 0.48 mL) and 4 eq. KF (4 mmol, 0.232 g) afforded 0.1849 g (93%) of 4,4'-diaminodiphenylmethane (**31**) as a yellow-orange solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50, then 0/100); mp = 89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.99 (d, J = 8.24 Hz, 4H), 6.61 (d, J = 8.24 Hz, 4H), 3.79 (s, 2H), 3.54 (bs, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.1, 131.7, 129.4, 115.1, 40.0. Physical and spectral data were consistent with commercially available material.



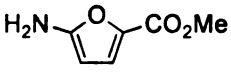
Subjection of bis(4-nitrophenyl)methane (1 mmol, 0.258 g) to the general procedure for reducing nitro arenes with 3 equiv of PMHS (3 mmol, 0.18 mL) afforded 0.0591 g (30%) of 4,4'-diaminodiphenylmethane, and 0.1101 g (48%) of 4-(4-nitrobenzyl)aniline as a white solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50, then 0/100); mp = 176 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (d, J = 8.79 Hz, 2H), 7.28 (d, J = 8.24 Hz, 2H), 6.92 (d, J = 8.24 Hz, 2H), 6.61 (d, J = 8.24 Hz, 2H), 3.93 (s, 2H), 3.59 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.7, 146.2, 145.0, 129.8, 129.4, 129.0, 123.6, 115.3, 40.0. Physical and spectral data were consistent with commercially available material.



4-Methoxybenzene-1,3-diamine: Subjection of 1-methoxy-2,4-dinitrobenzene (1 mmol, 0.198 g) to the general procedure for reducing nitro arenes with 8 equiv of PMHS (8 mmol, 0.48 mL) and 4 equiv KF (4 mmol, 0.232 g) afforded 0.1224 g (89%) of 4-methoxybenzene-1,3-diamine as a tan solid (silica gel FC, hexanes/EtOAc: 50/50, then 0/100); mp = 65 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.58 (d, *J* = 7.69 Hz, 1H), 6.03 (m, 2H), 3.73 (s, 3H), 3.54 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.6, 136.9, 112.1, 104.5, 103.2, 56.0. Physical and spectral data were consistent with commercially available material.

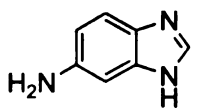


2,4-diaminobenzonitrile: Subjection of 2,4-dinitrobenzonitrile (1 mmol, 0.193 g) to the general procedure for reducing nitro arenes with 8 equiv of PMHS (8 mmol, 0.48 mL) and 4 equiv KF (4 mmol, 0.232 g) afforded a complex mixture of products. All starting material was consumed.



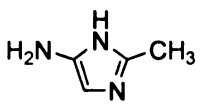
Methyl 5-amino-2-furoate: Subjection of methyl 5-nitro-2-furoate (1 mmol, 0.171 g) to the general procedure for reducing nitro arenes afforded 0.124 g (89%) of methyl 5-amino-2-furoate as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 134–135°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.02 (d, *J* = 3.29 Hz, 1H), 6.41 (bs, 2H), 5.01 (d, *J* = 3.29 Hz, 1H), 3.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.7, 158.0, 132.2,

123.6, 84.2, 50.4. Physical and spectral data were consistent with those previously reported.[156]

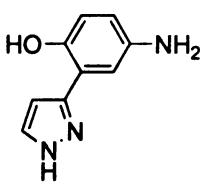


6-Amino-*1H*-benzimidazole: A dry 25 mL round bottom was charged with $Pd(OAc)_2$ (0.05 mmol, 0.011 g), sealed, and placed under a positive pressure of nitrogen. Dry THF (5 mL) and aqueous KF (2 mmol, 0.116 g, in 2 mL of degassed water) were added sequentially. PMHS (0.67 mmol, 0.04 mL) was added dropwise via syringe and the reaction was stirred ~15–45 seconds to preform the PMHS-$Pd(OAc)_2$ nanoparticles. The reaction was then opened (to the air) and 6-nitro-*1H*-benzimidazole (1 mmol, 0.163 g) was added quickly in a single portion. The reaction flask was resealed and purged with nitrogen and the remaining PMHS (3.3 mmol, 0.20 mL) was added dropwise. The nitrogen inlet was replaced by a balloon of nitrogen. The reaction was stirred for 30 min. Following the general extraction protocol, the organics were filtered though a plug of Celite. Concentration of the crude material and flash chromatography afforded 0.1331 g (89%, containing residual (~10 %) H_2O) of 6-amino-1H-benzimidazole as a cream colored solid (silica gel FC, EtOAc/MeOH: 100/0, 80/20, then 50/50); mp = 160–165°C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.85 (bs, 1H), 7.92 (s, 1H), 7.29 (d, J = 8.24 Hz, 1H), 6.71 (s, 1H), 6.54 (d, J = 8.24 Hz, 1H), 4.91 (bs, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 144.5, 139.6, 136.9, 132.9, 117.1, 111.6, 96.8. IR (MeOH solution) 3175, 2820, 1635, 1522, 1491, 1361, 1265, 1209, 1028, 949, 812, 619 cm^{-1}; LRMS (EI, 70 eV) 132, 116, 106, 105, 78, 66, 52; HRMS (EI) *m/z* calcd for $C_7H_7N_3$ 133.0640, found

133.0637. Physical and spectral data were consistent with those previously reported.[157] (Note: In lieu of opening the reaction system to the air 6-nitro-1H-benzimidazole can be dissolved in a THF (2 mL) water (1mL) mixture and added to the reaction via syringe.)

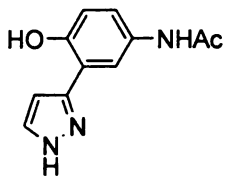


2-Methyl-*1H*-imidazol-5-amine: Subjection of 2-methyl-5-nitro-*1H*-imidazole (1 mmol, 0.127 g) to the general procedure for reducing nitro arenes afforded a complex mixture of products. All starting material was consumed.

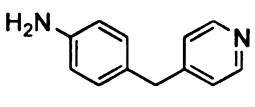


4-Amino-2-(1*H*-pyrazol-3-yl)phenol: A dry 25 mL round bottom was charged with $Pd(OAc)_2$ (0.05 mmol, 0.011 g), sealed, and placed under a positive pressure of nitrogen. Dry THF (5 mL) and aqueous KF (2 mmol, 0.116 g, in 2 mL of degassed water) were added sequentially. PMHS (0.67 mmol, 0.04 mL) was added dropwise via syringe and the reaction was stirred ~15–45 seconds to preform the PMHS-$Pd(OAc)_2$ nanoparticles. The reaction was then opened (to the air) and 4-nitro-2-(1H-pyrazol-3-yl)phenol (1 mmol, 0.205 g) was added quickly in a single portion. The reaction flask was resealed and purged with nitrogen and the remaining PMHS (3.3 mmol, 0.20 mL) was added dropwise. The nitrogen inlet was replaced by a balloon of nitrogen. The reaction was stirred for 30 min. Following the general extraction protocol, the organics were filtered though a plug of Celite, concentrated and subjected to flash chromatography afforded 0.1559g (89%) of 4-amino-2-(1*H*-pyrazol-3yl)phenol and 0.0086g (5%) of the oxidized product

(inseparable mixture), as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50 then EtOAc); mp = 160-165 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 10.15 (bs, 1H), 7.22 (d, *J* = 2.74 Hz, 1H), 6.61 (d, *J* = 2.74 Hz, 1H), 6.42 (m, 1H), 6.23 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 149.8, 147.4, 138.3, 128.7, 116.2, 116.0, 115.8, 112.0, 100.5.

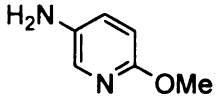


Analytically pure material was obtained by following the general procedure for reduction of nitro arenes with the following modification. After complete consumption of the starting material (as judged by TLC) acetic anhydride (2 mmol, 0.188 mL) was added to the reaction mixture followed by an additional 30 minutes of stirring to afford after the general workup 0.1892 g (87%) of *N*-(4-hydroxy-3-(1*H*-pyrazol-3-yl)phenyl)acetamide as a white solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50 then 0/100); mp = 172-176 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 10.37 (bs, 1H), 8.99 (s, 1H), 7.37 (d, *J* = 2.74 Hz, 1H), 7.07 (d, *J* = 2.74 Hz, 1H), 6.78 (dd, *J* = 2.19 and 8.79 Hz, 1H), 6.33 (d, *J* = 8.79 Hz, 1 H), 6.06 (d, *J* = 2.19 Hz, 1H), 1.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + d_6-DMSO): δ 167.4, 150.7, 149.1, 129.7, 128.6, 120.1, 117.3, 115.4, 115.3, 100.2, 22.7; HRMS (EI) *m/z* calcd for $C_{11}H_{11}N_3O_2$ 217.0851, found 217.0848.

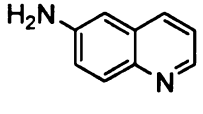


4-(Pyridin-4-ylmethyl)aniline: Subjection of 4-(4-nitrobenzyl)pyridine (1 mmol, 0.214 g) to the general procedure for reducing nitro arenes afforded 0.1831 g (99%) of 4-(pyridin-4-ylmethyl)aniline as a white solid (silica gel FC, hexanes/EtOAc: 50/50 then

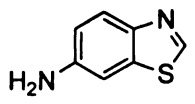
0/100); mp = 157 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 8.17 (d, *J* = 6.04 Hz, 2H), 6.82 (d, *J* = 6.04 Hz, 2H), 6.66 (d, *J* = 8.24 Hz, 2H), 6.36 (d, *J* = 8.24 Hz, 2H), 3.69 (bs, 2H), 3.56 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + d_6-DMSO): δ 150.4, 148.9, 144.9, 129.1, 127.3, 123.4, 114.5. Physical and spectral data were consistent with commercially available material.



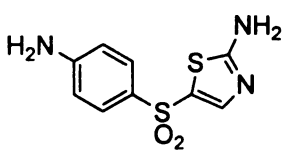
6-Methoxypyridin-3-amine: Subjection of 2-methoxy-5-nitropyridine (1 mmol, 0.154 g) to the general procedure for reducing nitro arenes afforded 0.124 g (100%) of 6-methoxypyridin-3-amine as an amber oil (silica gel FC, hexanes/EtOAc: 50/50 then 0/100); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (d, *J* = 2.74 Hz, 1H), 6.93 (dd, *J* = 2.74 and 8.79 Hz, 1H), 6.52 (d, *J* = 8.79 Hz, 1H), 3.78 (s, 3H), 3.38 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.8, 136.6, 132.6, 127.4, 110.5, 53.1. Physical and spectral data were consistent with commercially available material.



Quinolin-6-amine: Subjection of 6-nitroquinoline (1 mmol, 0.174 g) to the general procedure for reducing nitro arenes afforded 0.144 g (100%) of quinolin-6-amine as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50 then 0/100); mp = 118-120 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.57 (dd, *J* = 1.64 & 4.39 Hz, 1H), 7.83 (d, *J* = 8.79 Hz, 1H), 7.77 (d, *J* = 8.24 Hz, 1H), 7.16 (dd, *J* = 4.39 & 8.24 Hz, 1H), 7.05 (dd, *J* = 2.74 & 8.79 Hz, 1H), 6.77 (d, *J* = 2.74 Hz, 1H), 4.04 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.4, 144.6, 143.1, 133.6, 130.1, 129.6, 121.4, 121.1, 107.1. Physical and spectral data were consistent with commercially available material.

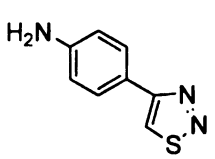


6-Amino-*1H*-thioimidazole: A dry 25 mL round bottom was charged with $Pd(OAc)_2$ (0.05 mmol, 0.011 g), sealed, and placed under a positive pressure of nitrogen. Dry THF (3 mL) and aqueous KF (2 mmol, 0.116 g, in 1.5 mL of degassed water) were added sequentially. PMHS (0.67 mmol, 0.04 mL) was added dropwise via syringe and the reaction was stirred ~15–45 seconds to preform the PMHS-$Pd(OAc)_2$ nanoparticles. At that point 6-nitrobenzothiazole (1mmol, 0.180 g) dissolved in 2 mL of dry THF and 0.5 mL H_2O was injected, followed by the dropwise addition of the remaining PMHS (3.3 mmol, 0.20 mL). The nitrogen inlet was replaced by a balloon of nitrogen. The reaction was stirred for 30 min. Following the general extraction protocol, the organics were filtered though a plug of Celite, concentrated and subjected to flash chromatography affording 0.1069 g (~71%, material is contaminated with unknown material) of 6-amino-*1H*-thioimidazole as a yellow solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50 then 0/100); ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.13 (s, 1H), 7.76 (s, 1H), 7.54 (s, 1H), 7.14 (d, J = 8.79 Hz, 1H), 6.81 (s, 1H), 6.34 (d, J = 8.79 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 149.0, 148.8, 145.9, 133.3, 121.2, 119.0, 112.2, 102.6.

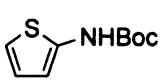


5-(4-Aminophenylsulfonyl)thiazol-2-amine: A dry 25 mL round bottom was charged with $Pd(OAc)_2$ (0.05 mmol, 0.011 g), sealed, and placed under a positive pressure of nitrogen. Dry THF (3 mL) and aqueous KF (2 mmol, 0.116 g, in 1.5 mL of

degassed water) were added sequentially. PMHS (0.67 mmol, 0.04 mL) was added dropwise via syringe and the reaction was stirred ~15–45 seconds to preform the PMHS-$Pd(OAc)_2$ nanoparticles. At that point 2-amino-5-(4-nitrophenylsulfonyl)thiazole (1mmol, 0.285 g) dissolved in 2 mL of dry THF and 0.5 mL H_2O was injected, followed by the dropwise addition of the remaining PMHS (3.3 mmol, 0.20 mL). The nitrogen inlet was replaced by a balloon of nitrogen. The reaction was stirred for 30 min. Following the general extraction protocol, the organics were filtered though a plug of Celite, concentrated and subjected to flash chromatography affording 0.2405 g (94%) of 5-(4-aminophenylsulfonyl)thiazol-2-amine as a yellow solid (silica gel FC, hexanes/EtOAc: 50/50 then 0/100); mp = 173 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.05 (s, 1H), 8.70 (s, 1H), 7.85 (bs, 2H), 7.58 (d, J = 8.79 Hz, 2H), 7.46 (s, 0.5H), 6.84 (d, J = 8.79 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 174.2, 155.7, 145.9, 130.6, 127.9, 123.7, 111.4; IR (Nujol) 3414, 3312, 1595, 1485, 1294, 1219, 1142, 1095, 1035, 702 cm^{-1}; HRMS (EI) *m/z* calcd for $C_9H_9N_3O_2S_2$ 255.0136, found 255.0133



4-(1,2,3-Thiadiazol-4-yl)aniline: Subjection of 4-(4-nitrophenyl)-1,2,3-thiadiazole (1 mmol, 0.207 g) to the general procedure for reducing nitro arenes afforded a complex mixture of products. All starting material was consumed.



2-Aminothiophene: 2-Nitrothiophene[158] (1 mmol, 0.129 g) was subjected to the general procedure for reducing nitro arenes with the following

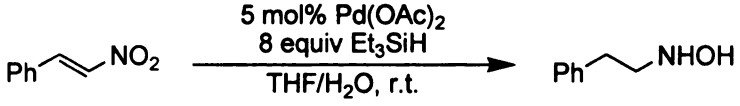
modification. After complete consumption of the starting material (as judged by TLC) di(*tert*-butyl)dicarbonate (2 mmol, 0.436 g) dissolved in 0.5 mL THF was injected into the reaction followed by an additional 4 hours of stirring. Following the general extraction protocol, the organics were filtered though a plug of Celite. Concentration of the crude material and flash chromatography afforded 0.1614 g (81%) of *tert*-butyl thiophen-2-ylcarbamate as a white solid (silica gel FC, hexanes/EtOAc: 95/5 then 80/20); mp = 150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.91 (bs, 1H), 6.78 (m, 2H), 6.49 (dd, *J* = 1.64, 3.29 Hz, 1H), 1.49 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.4, 140.2, 124.3, 116.9, 111.1, 81.3, 28.2. Physical and spectral data were consistent with those previously reported.[159] (2-aminothiophene decomposes immediately when exposed to air, so the reaction system should not be opened to the air until the amine is protected.)

General Procedure E

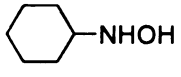
General Procedure for the Reduction of Aliphatic Nitro Compounds: A round bottom flask was charged with palladium acetate (0.05 mmol, 11 mg), the nitroarene (1 mmol), and freshly distilled dry THF (5 mL). The flask was sealed and purged with nitrogen. While purging the flask with nitrogen 2 mL of degassed water were injected via syringe. The nitrogen inlet was replaced with a balloon of nitrogen. Triethylsilane (6 mmol, 0.96 mL) was slowly added dropwise via syringe. The reaction was stirred for 2 hours or until complete as judged by TLC. At that time, the reaction flask was opened to the air and diluted with 5-10 mL of diethyl ether. The layers were separated and the aqueous layer was back extracted with diethyl ether. The combined organics were concentrated and subjected to flash chromatography using gradients of hexanes/EtOAc and /or EtOAc/MeOH.

 ***N*-Decylhydroxylamine**: Subjection of 1-nitrodecane[160] (1 mmol, 0.187 g) to the general procedure for reducing aliphatic nitro compounds afforded 0.1447 g (83%) of *N*-decylhydroxylamine as a white solid (silica gel FC, hexanes/EtOAc: 90/10 then 0/100); m.p. = 79 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.24 (bs, 2H), 2.90 (t, *J* = 7.14 Hz, 2H), 1.49 (m, 2H), 1.22 (m, 14H), 0.84 (t, *J* = 7.14 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.9, 31.9, 29.5, 29.3, 27.1, 26.9, 22.6, 14.1; IR (KBr) 3270, 3159, 2931, 2865, 1473, 1153, 1061, 891, 721 cm^{-1}; LRMS (EI, 70 eV) 173 (3), 157 (3), 142 (1), 70 (19), 46 (100); HRMS (EI) *m/z* calcd for $C_{10}H_{23}N_3O$ 173.1780, found 173.1781.

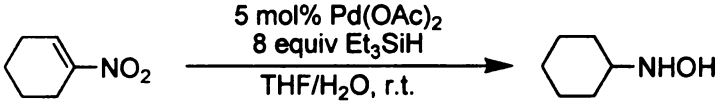
 ***N*-Phenethylhydroxylamine**: Subjection of (2-nitroethyl)benzene (1 mmol, 0.151 g) to the general procedure for reducing aliphatic nitro compounds afforded 0.0803 g (58%) of *N*-phenethylhydroxylamine as a white solid (silica gel FC, EtOAc/MeOH: 100/0 then 80/20); m.p. = 85 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29 (m, 2H), 7.22 (m, 3H), 6.33 (bs, 2H), 3.17 (t, *J* = 7.14 Hz, 2H), 2.87 (t, *J* = 7.14 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.0, 128.7, 128.5, 126.2, 54.7, 33.1; IR (neat) 3246, 3152, 2862, 1496, 1454, 1059, 740, 696 cm^{-1}; LRMS (EI, 70 eV) 137 (1), 136 (1), 121 (8), 105 (13), 104 (24), 92 (83), 91 (100), 77 (13), 76 (17), 46 (32), 45 (34); HRMS (EI) *m/z* calcd for $C_8H_{11}NO$ 137.0841, found 137.0843.



Trans-β-Nitrostyrene (1 mmol, 0.149 g) was subjected to the general procedure for reducing aliphatic nitro compounds with 8 equivalents of triethylsilane (8 mmol, 1.28 mL) affording 0.0728 g (53%) of *N*-phenethylhydroxylamine.

 ***N*-Hydroxylaminocyclohexane**: Nitrocyclohexane (1 mmol, 0.122 mL) was subjected to the general procedure for reducing aliphatic nitro compounds with the following modification. After complete consumption of the starting material (as judged by TLC) 2 equiv *p*-toluenesulfonic anhydride (2 mmol, 0.652 g) was added to the reaction followed by an additional 2 hours of stirring to afford after the general workup 0.2388 g (89%) of *N*-cyclohexyl-*N*-hydroxy-4-methyl-benzenesulfonamide as a white solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); mp = 127-129 °C. ^{1}H NMR (300 MHz,

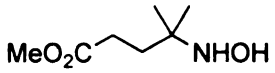
$CDCl_3$): δ 7.81 (d, *J* = 8.24 Hz, 2H), 7.29 (d, *J* = 8.24 Hz, 2H), 6.64 (s, 1H), 3.62 (tt, *J* = 3.84, 10.98 Hz, 1H), 2.41 (s, 3H), 1.72–0.85 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.3, 133.8, 129.5, 128.8, 60.3, 28.9, 25.3, 25.2, 21.6; IR (PTFE card) 3366, 2930, 2855, 1334, 1185, 1082, 665, 584 cm^{-1}; LRMS (EI, 70 eV) 269 (1), 253 (3), 157 (78), 139 (46), 91 (100), 83 (44), 77 (7), 76 (9), 55 (46), 54 (44), 41 (53); HRMS (EI) *m/z* calcd for $C_{13}H_{19}NO_3S$ 269.1086, found 269.1090



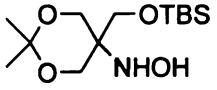
1-Nitro-1-cylcohexene (1 mmol, 0.113 mL) was subjected to the general procedure for reducing aliphatic nitro compounds with 8 equivalents of triethylsilane (8 mmol, 1.28 mL) with the following modification. After complete consumption of the starting material (as judged by TLC) 2 equiv *p*-toluenesulfonic anhydride (2 mmol, 0.652 g) was added to the reaction followed by an additional 2 hours of stirring afforded 0.237 g (88%) of *N*-cyclohexyl-*N*-hydroxy-4-methyl-benzenesulfonamide.

$(AcOCH_2)_3C$-NHOH **1,3-Diacetoxy-2-acetoxymethyl-2-(*N*-hydroxy)aminopropane**: Subjection of 1,3-diacetoxy-2-acetoxymethyl-2-nitropropane[161] (1 mmol, 0.277 g) to the general procedure for reducing aliphatic nitro compounds afforded 0.0819 g (31%) of 1,3-diacetoxy-2-acetoxymethyl-2-(*N*-hydroxy)aminopropane as a clear oil. ^1H NMR (300 MHz, $CDCl_3$): δ 5.21 (bs, 2H), 4.14 (s, 6H), 2.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8, 62.0, 61.0, 20.7; IR (neat) 3372, 2963, 1734, 1653, 1437, 1379, 1226, 1047, 952, 908 cm^{-1};

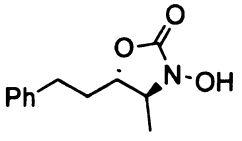
LRMS (EI, 70 eV) 263 (0.5), 232 (40), 190 (30), 172 (9), 113 (74), 102 (13), 54 (7), 43 (100); HRMS (EI) *m/z* calcd for $C_{10}H_{17}NO_7$ 263.1005, found 269.0997.



Methyl 4-(*N*-hydroxy)amino-4-methylpentanoate: Subjection of methyl 4-methyl-4-nitropentanoate (1 mmol, 0.157 mL) to the general procedure for reducing aliphatic nitro compounds afforded trace amounts (~1 mg) of methyl 4-(*N*-hydroxy)amino-4-methylpentanoate along with 0.1119 g (64%) of starting material recovered.



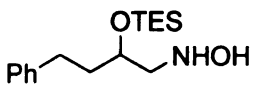
***N*-(5-((tert-butyldimethylsilyloxy)methyl)-2,2-dimethyl-1,3-dioxan-5-yl)hydroxylamine**: Subjection of tert-butyl((2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)methoxy)dimethylsilane (1 mmol, 0.305 g) to the general procedure for reducing aliphatic nitro compounds afforded no product along with 0.234g (77%) of starting material recovered.



1.8/1 anti/syn

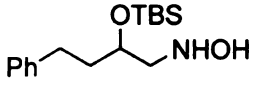
3-Hydroxy-4-methyl-5-phenethyloxazolidin-2-one: 4-Nitro-1-phenyl-3-pentanol[162] (1 mmol, 0.209 g, syn/anti mixture = 1.77/1) was subjected to the general procedure for reducing aliphatic nitro compounds with the following modification. After stirring for 4 hours the starting material was completely consumed (as judged by TLC). At that time 2 equiv of *N,N'*-carbonyldiimidazole (2 mmol, 0.324 g) was added and the reaction was stirred an additional 6 hours to afford after the general workup 0.1822 g (89%) of 3-hydroxy-4-methyl-5-phenethyloxazolidin-2-one (anti/syn = 1.8/1) as clear solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.76 (bs, 1H), 7.32–7.12 (m, 5H), 4.43 (ddd, J = 3.84, 7.14, 10.43 Hz, 0.35H), 3.96 (m, 1H), 3.55 (dq, J = 2.19,

6.04 Hz, 0.63H), 2.85 (m, 1H), 2.66 (m, 1H), 2.10–1.73 (m, 2H), 1.29 (d, J = 6.04 Hz, 2.04H), 1.20 (d, J = 6.59 Hz, 1.14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.5, 160.4, 140.2, 140.1, 128.5, 128.4, 128.3, 126.2, 79.8, 76.0, 60.5, 57.8, 34.5, 31.3, 30.9, 16.0; IR (neat) 3267, 2936, 1757, 1496, 1456, 1387, 1228, 1111, 1035, 752, 700 cm^{-1}; LRMS (EI, 70 eV) 221 (20), 220 (13), 204 (12), 146 (9), 116 (39), 105 (44), 104 (67), 99 (15), 91 (100), 77 (50), 41 (100); HRMS (EI) *m/z* calcd for $C_{12}H_{15}NO_3$ 221.1052, found 221.1055. Spectral data were similar to those previously reported for the oxazolidinone.[163]



_N_-(4-Phenyl-2-(triethylsilyloxy)butyl)hydroxylamine: Subjection of triethyl(1-nitro-4-phenylbutan-2-yloxy)silane (1 mmol, 0.309 g) to the general procedure for reducing aliphatic nitro compounds with 10 equiv triethylsilane (10 mmol, 1.6 mL) afforded 0.1646 g (56%) of *N*-(4-phenyl-2-(triethylsilyloxy)butyl)hydroxylamine as a light yellow oil, and 0.1178 g (38%) of starting material (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (m, 2H), 7.19 (m, 2H), 6.16 (bs, 2H), 4.07 (m, 1H), 3.04 (dd, J_{AA} = 3.84 Hz, J_{AB} = 3.29 Hz, 1H), 2.92 (dd, J_{BB} = 7.14 Hz, J_{BA} = 7.69 Hz, 1H), 2.66 (t, J = 8.79 Hz, 2H), 1.83 (m, 2H), 0.99 (t, J = 8.24 Hz, 6H), 0.65 (q, J = 8.24 Hz, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.0, 128.3, 128.2, 125.7, 68.4, 59.0, 37.6, 31.4, 6.8, 4.9; IR (neat) 3267, 2953, 2930, 2856, 1471, 1255, 1097, 1068, 837, 777, 698 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{16}H_{29}NO_2Si$ 295.1968, found 295.1964.

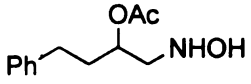
Subjection of triethyl(1-nitro-4-phenylbutan-2-yloxy)silane (1 mmol, 0.309 g) to the general procedure for reducing aliphatic nitro compounds afforded 0.1287 g (44%) of *N*-(4-phenyl-2-(triethylsilyloxy)butyl)hydroxylamine as a light yellow oil and 0.1573 g (51%) of starting material



***N*-(2-(*tert*-Butyldimethylsilyloxy)-4-phenylbutyl) hydroxylamine**: Subjection of *tert*-butyldimethyl(1-nitro-4-phenylbutan-2-yloxy)silane (1 mmol, 0.309 g) to the general procedure for reducing aliphatic nitro compounds with 10 equiv triethylsilane (10 mmol, 1.6 mL) afforded 0.1685 g (57%) of *N*-(2-(*tert*-butyldimethylsilyloxy)-4-phenylbutyl)hydroxylamine as a light yellow oil, and 0.0966 g (31%) of starting material (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.14 (m, 5H), 6.29 (bs, 2H), 4.06 (m, 1H), 3.03 (dd, J_{AA} = 3.84 Hz, J_{AB} = 3.29 Hz, 1H), 2.94 (dd, J_{BB} = 7.14 Hz, J_{BA} = 7.14 Hz, 1H), 2.64 (t, J = 7.69 Hz, 2H), 1.81 (m, 2H), 0.96 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.1, 128.3, 128.2, 125.7, 68.3, 59.0, 37.6, 31.3, 25.8, 18.0, -4.4, -4.6; IR (neat) 3267, 2953, 2930, 2856, 1471, 1255, 1097, 1068, 837, 777, 698 cm^{-1}; LRMS (EI, 70eV) 249 (24), 248 (10), 147 (6), 132 (5), 131 (35), 117 (36), 115 (14), 91 (83), 77 (6), 75 (63), 74 (15), 73 (100), 72 (11), 57 (10); HRMS (EI) *m/z* calcd for $C_{16}H_{29}NO_2Si$ 295.1968, found 295.1974.

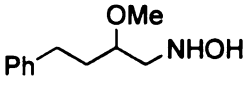
Subjection of *tert*-butyldimethyl(1-nitro-4-phenylbutan-2-yloxy)silane (1 mmol, 0.309 g) to the general procedure for reducing aliphatic nitro compounds afforded

0.1327 g (45%) of *N*-(2-(*tert*-butyldimethylsilyloxy)-4-phenylbutyl)hydroxylamine as a light yellow oil, and 0.1321 g (42%) of starting material.



1-(Hydroxyamino)-4-phenylbutan-2-yl acetate: Subjection of 1-nitro-4-phenylbutan-2-yl acetate (1 mmol, 0.237 g) to the general procedure for reducing aliphatic nitro compounds with 10 equiv triethylsilane (10 mmol, 1.6 mL) afforded 0.1214 g (54%) of 1-(hydroxyamino)-4-phenylbutan-2-yl acetate as an orange solid (silica gel FC, hexanes/EtOAc: 50/50, 0/100 then 80/20 (EtOAc/MeOH)); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20 (m, 5H), 3.91 (m, 1H), 3.46 (m, 1H), 2.74 (m, 2H), 2.09 (s, 3H), 1.73 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.1, 141.4, 128.29, 128.25, 125.8, 68.5, 66.6, 57.1, 54.1, 36.0, 35.6, 31.6, 20.1.

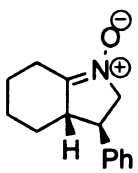
Subjection of 1-nitro-4-phenylbutan-2-yl acetate (1 mmol, 0.237 g) to the general procedure for reducing aliphatic nitro compounds afforded 0.1098 g (49%) of 1-(hydroxyamino)-4-phenylbutan-2-yl acetate.



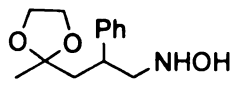
***N*-(2-Methoxy-4-phenylbutyl)hydroxylamine**: Subjection of (3-methoxy-4-nitrobutyl)benzene (1 mmol, 0.209 g) to the general procedure for reducing aliphatic nitro compounds with 10 equiv triethylsilane (10 mmol, 1.6 mL) afforded 0.1647 g (84%) of *N*-(2-methoxy-4-phenylbutyl)hydroxylamine as a clear oil (silica gel FC, hexanes/EtOAc: 50/50, 0/100 then 80/20 (EtOAc/MeOH)); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.12 (m, 5H), 6.28 (bs, 2H), 3.51 (m, 1H), 3.39 (s, 3H), 3.05 (dd, J_{AA} = 3.29 Hz, J_{AB} = 3.84 Hz, 1H), 2.91 (dd, J_{BB} = 8.24 Hz, J_{BA} = 7.69 Hz, 1H), 2.66 (t, J = 7.69 Hz, 2H),

1.82 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.8, 128.3, 128.2, 125.8, 76.7, 57.0, 56.7, 33.6, 31.2; IR (neat) 3267, 3026, 2930, 2828, 1496, 1456, 1103, 1057, 910, 733 cm^{-1}; LRMS (EI, 70eV) 149 (9), 131(6), 118 (4), 117 (29), 105 (6), 91 (100), 77 (5); HRMS (EI) *m/z* calcd for $C_{11}H_{17}NO_2$ 195.1259, found 195.1258.

Subjection of (3-methoxy-4-nitrobutyl)benzene (1 mmol, 0.209 g) to the general procedure for reducing aliphatic nitro compounds afforded 0.1089 g (56%) of *N*-(2-methoxy-4-phenylbutyl)hydroxylamine



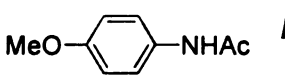
3-Phenyl-3,3a,4,5,6,7-hexahydro-2*H*-indole-1-oxide: Subjection of *syn*-2-(2-nitro-1-phenyl-ethyl)-cyclohexanone[164] (1 mmol, 0.247 g) to the general procedure for reducing aliphatic nitro compounds with 10 equiv triethylsilane (10 mmol, 1.6 mL) afforded 0.165 g (77%) of the nitrone 3-phenyl-3,3a,4,5,6,7-hexahydro-2*H*-indole-1-oxide as an amber oil (silica gel FC, EtOAc/MeOH: 100/0, 90/10, the 80/20). ^1H NMR (300 MHz, $CDCl_3$): δ 7.36–7.11 (m, 5H), 4.30–4.03 (m, 2H), 3.18 (m, 2H), 2.76 (m, 1H), 2.12–1.85 (m, 3H), 1.79 (m, 1H), 1.45–1.09 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.9, 139.7, 128.9, 127.3, 127.1, 68.1, 50.5, 45.7, 32.2, 24.1, 23.7, 23.4; IR (neat) 3391, 2937, 2860, 2206, 1624, 1498, 1448, 1379, 1251, 1230, 1180, 925, 731 cm^{-1}; LRMS (EI, 70 eV) 215 (64), 198 (18), 111 (73), 104 (18), 91 (38), 84 (23), 77 (23); HRMS (EI) *m/z* calcd for $C_{14}H_{17}NO$ 215.1310, found 215.1307. Spectral data were similar to those previously reported for a related nitrone.[165]



***N*-(3-(2-Methyl-1,3-dioxolan-2-yl)-2-phenylpropyl) hydroxylamine**: Subjection of 2-methyl-2-(3-nitro-2-phenylpropyl)-1,3-dioxolane (1mmol, 0.251 g) to the general procedure for reducing aliphatic nitro compounds afforded 0.121 g (51%) of *N*-(3-(2-Methyl-1,3-dioxolan-2-yl)-2-phenylpropyl)hydroxylamine as a clear oil (silica gel FC, hexanes/EtOAc: 50/50, 0/100 then 70/30 (EtOAc/MeOH)); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29-7.08 (m, 5H), 5.60 (bs, 2H), 3.83 (m, 4H), 3.17 (m, 2H), 2.92 (m, 1H), 2.00 (m, 2H), 1.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.9, 128.5, 127.7, 126.4, 109.7, 64.4, 64.2, 59.9, 42.8, 38.2, 24.4; IR (neat) 3410, 3271, 2982, 2941, 2885, 1495, 1454, 1379, 1251, 1221, 1143, 1076, 1049, 910, 734, 702 cm^{-1}; LRMS (EI, 70eV) 175 (6), 161 (2), 160 (2), 159 (2), 158 (5), 118 (2), 117 (7), 116 (2), 115 (6), 104 (12), 91 (11), 88 (17), 87 (100), 86 (38), 77 (5), 43 (80); HRMS (Chem Ion) *m/z* calcd for $[C_{13}H_{19}NO_3 + H]^+$ 238.1443, found 238.1434.

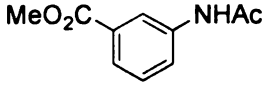
General Procedure F

General Procedure for the one-pot reductive conversion of nitroarenes to amides, carbamates, or sulfonamides: A round bottom flask was charged with palladium acetate (0.05 mmol, 11 mg), the nitroarene (1 mmol), and freshly distilled dry THF (5 mL). The flask was sealed and purged with nitrogen. While purging the flask with nitrogen a solution of aqueous KF was added via syringe (2 mmol KF, 116 mg; in 2 mL of degassed water). The nitrogen inlet was replaced with a balloon of nitrogen. PMHS (4 mmol, 0.24 mL; 1 mmol of hydride is 0.06mL) was slowly added dropwise via syringe (*Caution: Rapid addition PMHS can result in uncontrollable gas evolution!*) The reaction was stirred for 30 min or until complete as judged by TLC. At that time, the reaction flask was opened to the air and the anhydride (2 mmol), sulfonic anhydride (2 mmol), or dicarbonate (2 mmol) was added quickly, followed by resealing the round bottom and flushing with nitrogen. The anhydride (or dicarbonate) can also be dissolved in 0.5 mL of THF an injected into the reaction mixture without opening up the round bottom. The reaction was stirred for an additional 30 min or until complete as judged by TLC. The layers were separated and the aqueous layer was back extracted with diethyl ether. The combined organics were concentrated and subjected to flash chromatography using gradients of hexanes/EtOAc and/or EtOAc/MeOH.

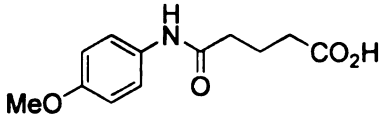


***N*-(4-Methoxyphenyl)acetamide**: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with acetic anhydride (2 mmol, 0.188 mL) afforded 0.1635 g (99%) of *N*-(4-methoxyphenyl)acetamide as a white solid (silica gel FC, hexanes/EtOAc: 50/50 then 0/100); mp = 129 °C; ^{1}H

NMR (300 MHz, $CDCl_3$): δ 8.72 (s, 1H), 7.31 (d, *J* = 8.79 Hz, 2H), 6.67 (d, *J* = 8.79 Hz, 2H), 3.63 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.6, 155.7, 131.3, 121.6, 113.5, 55.1, 23.7. Physical and spectral data were consistent with commercially available material.

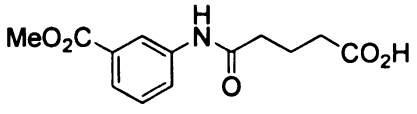


Methyl 3-acetamidobenzoate: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with acetic anhydride (2 mmol, 0.188 mL) afforded 0.193 g (100%) of methyl 3-acetamidobenzoate as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 136 °C; ^1H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 9.48 (s, 1H), 8.04 (s, 1H), 7.77 (d, *J* = 8.24 Hz, 1H), 7.56 (d, *J* = 7.69 Hz, 1H), 7.20 (dd, *J* = 7.69 and 8.24 Hz, 1H), 3.73 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + d_6-DMSO): δ 168.8, 166.2, 138.6, 129.8, 128.2, 123.9, 123.7, 120.1, 51.4, 23.6. Physical and spectral data were consistent with commercially available material.

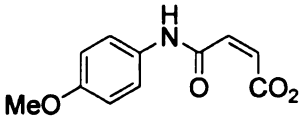


5-(4-Methoxyphenylamino)-5-oxopentanoic acid: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with glutaric anhydride (2 mmol, 0.228 g) afforded 0.2279 g (96%) of 5-(4-methoxyphenylamino)-5-oxopentanoic acid as a white solid (silica gel FC, hexanes/EtOAc: 50/50 then 0/100); mp = 140 °C; ^1H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 9.34 (s, 1H), 7.36 (d, *J* = 8.79 Hz, 2H), 6.67 (d, *J* = 8.79 Hz, 2H), 3.62 (s, 3H), 2.21 (m, 4H), 1.82 (q, *J* = 7.14 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + d_6-DMSO): δ 174.6, 170.6, 155.3, 132.0, 121.1, 113.4, 55.0, 35.5, 33.1, 20.6; IR (Nujol) 3314, 1695, 1658, 1541, 1516, 1458, 1414, 1304, 1267, 1236,

1186, 1033, 846, 808 cm^{-1}; LRMS (EI, 70 eV) 237 (12), 123 (100), 108 (65), 92 (3), 87 (6), 77 (2), 45 (9), 43 (4), 42 (5), 41 (10); HRMS (EI) *m/z* calcd for $C_{12}H_{15}NO_4$ 237.1001, found 237.1001

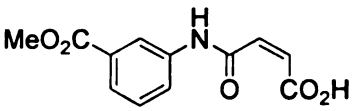


5-(3-(Methoxycarbonyl)phenylamino)-5-oxopentanoic acid: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with glutaric anhydride (2 mmol, 0.228 g) afforded 0.2296 g (87%) of 5-(3-(methoxycarbonyl)phenylamino)-5-oxopentanoic acid as a white solid (silica gel FC, hexanes/EtOAc: 80/20, 50/50 then 0/100); mp = 110 °C; ^1H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 8.98 (bs, 1H), 8.02 (s, 1H), 7.81 (d, *J* = 8.24 Hz, 1H), 7.60 (d, *J* = 7.69 Hz, 1H), 7.24 (dd, *J* = 7.69 and 8.24 Hz, 1H), 3.77 (s, 3H), 2.35 (t, *J* = 7.14 Hz, 2H), 2.29 (t, *J* = 7.14 Hz, 2H), 1.91 (q, *J* = 7.14 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + d_6-DMSO): δ 175.3, 171.3, 166.6, 138.7, 130.3, 128.6, 124.4, 124.0, 120.4, 51.8, 35.9, 33.0, 20.5; IR (Nujol) 3348, 3275, 1714, 1695, 1664, 1593, 1545, 1433, 1302, 1275, 1232, 1082, 925, 760, 688 cm^{-1}; LRMS (EI, 70eV) 265 (5), 151 (100), 120 (24), 119 (31), 115 (13), 93 (13), 92 (27), 91 (13), 90 (11), 87 (13), 86 (20), 77 (6), 59 (6) 45 (27), 44 (14), 43 (31), 42 (15), 41 (25); HRMS (EI) *m/z* calcd for $C_{13}H_{15}NO_5$ 265.0950, found 265.0948.



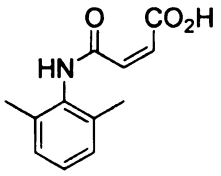
(*Z*)-4-(4-Methoxyphenylamino)-4-oxobut-2-enoic acid: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with maleic anhydride (2 mmol, 0.196 g) afforded 0.2109 g (95%) of (*Z*)-4-(4-methoxyphenylamino)-4-oxobut-2-enoic acid as a bright yellow

solid (silica gel FC, hexanes/EtOAc: 50/50 then 0/100); mp = 180 °C; ^{1}H NMR (300 MHz, d_6-DMSO): δ 10.40 (s, 1H), 7.51 (d, *J* = 8.79 Hz, 2H), 6.85 (d, *J* = 8.79 Hz, 2H), 6.44 (d, *J* = 12.08 Hz, 1H), 6.25 (d, *J* = 12.08 Hz, 1H), 3.66 (s, 3H); ^{13}C NMR (75 MHz, d_6-DMSO): δ 166.8, 163.2, 156.1, 132.0, 131.4, 131.3, 121.5, 114.1, 55.3; IR (Nujol) 3256, 3061, 1713, 1633, 1539, 1508, 1468, 1412, 1280, 1248, 1176, 1035, 854, 825 cm^{-1}; LRMS (EI, 70eV) 222 (1), 221 (11), 203 (27), 188 (12), 123 (69), 122 (44), 108 (100), 77 (8), 44 (6); HRMS (EI) *m/z* calcd for $C_{11}H_{11}NO_4$ 221.0688, found 221.0684.

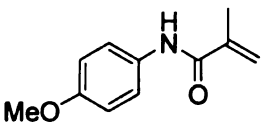


(Z)-4-(3-(Methoxycarbonyl)phenylamino)-4-oxobut-2-enoic acid: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with maleic anhydride (2 mmol, 0.196 g) afforded 0.2086 g (84%) of (Z)-4-(3-(methoxycarbonyl)phenylamino)-4-oxobut-2-enoic acid as a white solid (silica gel FC, EtOAc/MeOH: 100/0 then 80/20); mp = 170 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 10.90 (bs, 1H), 8.11 (s, 1H), 7.82 (d, *J* = 7.69 Hz, 1H), 7.67 (d, *J* = 8.24 Hz, 1H), 7.30 (dd, *J* = 7.69 and 8.24 Hz, 1H), 6.47 (d, J = 12.63 Hz, 1H), 6.19 (d, *J* = 12.63 Hz, 1H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + d_6-DMSO): δ 165.8, 165.4, 163.9, 137.3, 133.3, 132.5, 130.2, 128.6, 125.6, 124.6, 120.9, 51.7; IR (Nujol) 3317, 3157, 2926, 2855, 1724, 1628, 1591, 1558, 1496, 1296, 1257, 1203, 1105, 1082, 968, 893, 846, 760, 609 cm^{-1}; LRMS (EI, 70eV) 249 (6), 204 (5), 200 (36), 172 (20), 152 (11), 151 (51), 150 (71), 135 (1), 120 (45), 119 (70), 115 (10), 99 (12), 98 (18), 97 (10), 92 (100), 77 (5), 65 (16), 64 (32), 63 (16), 62

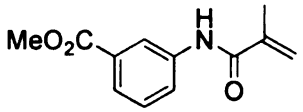
(15), 54 (26), 53 (36); HRMS (EI) *m/z* calcd for $C_{12}H_{11}NO_5$ 249.0637, found 249.0633.



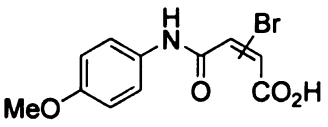
(Z)-4-(2,6-Dimethylphenylamino)-4-oxobut-2-enoic acid: Subjection of 2-nitro-*m*-xylene (1 mmol, 0.136 mL) to general procedure F with maleic anhydride (2 mmol, 0.196 g) afforded 0.063 g (29%) of (Z)-4-(2,6-dimethylphenylamino)-4-oxobut-2-enoic acid as a white solid (silica gel FC, EtOAc/MeOH: 100/0 then 80/20); mp = 170-173 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 9.94 (s, 1H), 6.53 (m, 3H), 6.15 (d, *J* = 13.18 Hz, 1H), 5.77 (d, *J* = 12.63 Hz, 1H), 1.65 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$ + d_6-DMSO): δ 163.9, 163.5, 133.6, 133.4, 131.6, 130.8, 126.8, 126.4, 17.0. Physical and spectral data were consistent with those previously reported.



***N*-(4-Methoxyphenyl)methacrylamide**: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with methacrylic anhydride (2 mmol, 0.296 mL) afforded 0.1894 g (99%) of *N*-(4-methoxyphenyl)methacrylamide as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 80 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43 (s, 1H), 7.43 (d, *J* = 8.79 Hz, 2H), 6.83 (d, *J* = 8.79 Hz, 2H), 5.75 (s, 1H), 5.40 (s, 1H), 3.76 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 156.4, 140.6, 130.8, 121.9, 119.5, 114.0, 55.3, 18.6; HRMS (EI) *m/z* calcd for $C_{11}H_{13}NO_2$ 191.0946, found 191.0941.

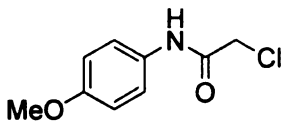


Methyl 3-methacrylamidobenzoate: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with methacrylic anhydride (2 mmol, 0.296 mL) afforded 0.2069 g (94%) of methyl 3-methacrylamidobenzoate as a light yellow oil (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (t, *J* = 1.64 Hz, 1H), 7.95 (bs, 1H), 7.89 (m, 1H), 7.72 (dt, *J* = 1.64, 8.24 Hz, 1H), 7.33 (t, *J* = 8.24 Hz, 1H), 5.77 (s, 1H), 5.42 (s, 1H), 3.83 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.8, 166.6, 140.5, 138.0, 130.7, 129.0, 125.3, 124.6, 121.0, 120.0, 52.1, 18.5; IR (neat) 3337, 2953, 1718, 1668, 1593, 1541, 1489, 1437, 1298, 1232, 1163, 1109, 929, 756 cm^{-1}; LRMS (EI, 70eV) 219 (6), 151 (23), 135 (1), 120 (10), 119 (5), 91 (10), 69 (100), 41 (75); HRMS (EI) *m/z* calcd for $C_{12}H_{13}NO_3$ 219.0895, found 219.0889.

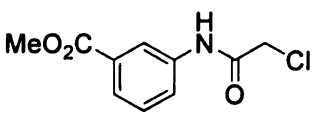


(E)-2-Bromo-4-(4-methoxyphenylamino)-4-oxobut-2-enoic acid and (E)-3-bromo-4-(4-methoxyphenylamino)-4-oxobut-2-enoic acid (1:1.26): Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with bromomaleic anhydride (2 mmol, 0.186 mL) afforded 0.2683 g (89%) of (E)-2-bromo-4-(4-methoxyphenylamino)-4-oxobut-2-enoic acid and (E)-3-bromo-4-(4-methoxyphenylamino)-4-oxobut-2-enoic acid (1:1.26) as a yellow-brown solid (silica gel FC, hexanes/EtOAc: 50/50 then 0/100); ^{1}H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 10.25 (s, 1H, measured 0.56H), 10.15 (s, 1H, measured 0.44H), 7.43 (d, *J* = 8.79 Hz, 2H), 6.76 (d, *J* = 9.33 Hz, 2H), 6.70 (s, 1H, measured 0.44H), 6.36 (s, 1H, measured 0.56H), 3.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ +

d_6-DMSO): δ 163.5, 161.3, 155.7, 131.8, 131.3, 125.3, 121.1, 120.7, 113.6, 113.5, 106.8, 66.5, 54.9, 28.7, 23.4.

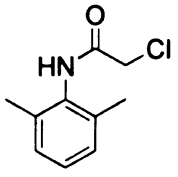


2-Chloro-*N*-(4-methoxyphenyl)acetamide: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with chloroacetic anhydride (2mmol, 0.341 g) afforded 0.1913 g (96%) of 2-chloro-*N*-(4-methoxyphenyl)acetamide as a white solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); mp = 117-119 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (bs, 1H), 7.41 (d, *J* = 8.79 Hz, 2H), 6.86 (d, *J* = 8.79 Hz, 2H), 4.14 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.6, 157.0, 129.6, 122.0, 114.2, 55.4, 42.8; IR (Nujol) 3294, 1674, 1545, 1512, 1466, 1414, 1300, 1248, 1180, 1030, 831, 788, 711, 688 cm^{-1}; LRMS (EI, 70eV) 201 (16), 200 (4), 199 (50), 124 (14), 123 (32), 122 (64), 121 (43), 108 (100), 77 (10); HRMS (EI) *m/z* calcd for $C_9H_{10}ClNO_2$ 199.0400, found 199.0397.

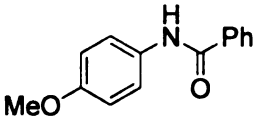


Methyl 3-(2-chloroacetamido)benzoate: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with chloroacetic anhydride (2 mmol, 0.341 g) afforded 0.1904 g (84%) of methyl 3-(2-chloroacetamido)benzoate as a tan solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); mp = 83 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (bs, 1H), 8.03 (m, 1H), 7.82 (dq, *J* = 1.09, 8.24 Hz, 1H), 7.74 (dt, *J* = 1.09, 7.69 Hz, 1H), 7.33 (dd, *J* = 7.69, 8.24 Hz, 1H), 4.13 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.4, 164.3, 136.9, 130.8, 129.1, 125.9, 124.5, 121.0, 52.1, 42.8; IR (Nujol) 1732, 1668, 1408, 1244, 1084, 814, 754 cm^{-1};

LRMS (EI, 70eV) 229 (9), 228 (3), 227 (28), 178 (21), 150 (99), 120 (100), 92 (67), 91 (26), 77 (11), 76 (17), 59 (4); HRMS (EI) *m/z* calcd for $C_{10}H_{10}ClNO_3$ 227.0349, found 227.0352

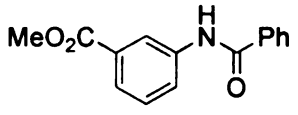


2-Chloro-*N*-(2,6-dimethylphenyl)acetamide: Subjection of nitro-*m*-xylene (1 mmol, 0.136 mL) to general procedure F with chloroacetic anhydride (2 mmol, 0.341 g) afforded 0.1439 g (<72%) of 2-chloro-*N*-(2,6-dimethylphenyl)acetamide, contaminated with unknown material, as a white-pink solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); mp = 114-117 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (bs, 1H), 7.08 (m, 3H), 4.22 (s, 2H), 2.21 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.3, 135.3, 128.3, 127.8, 107.9, 42.7, 18.2; IR (PTFE card, neat) 3254, 1662, 1533, 1177, 1142, 767 cm^{-1}; IR (Nujol) 3217, 1680, 1653, 1539, 1473, 1431, 1323, 1147, 979, 760, 707, 665 cm^{-1}; LRMS (EI, 70eV) 199 (7), 198 (2), 197 (21), 148 (100), 121 (31), 120 (23), 119 (36), 105 (24), 104 (16) 77 (40); HRMS (EI) *m/z* calcd for $C_{10}H_{12}ClNO$ 197.0607, found 197.0603.

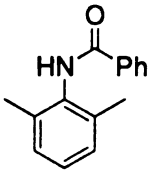


***N*-(4-Methoxyphenyl)benzamide**: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with benzoic anhydride (2 mmol, 0.452 g) afforded 0.22 g (97%) of *N*-(4-methoxyphenyl)benzamide as a white solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.51 (bs, 1H), 7.85 (d, *J* = 6.59 Hz, 2H), 7.56 (d, *J* = 8.79 Hz, 2H), 7.37 (m, 3H), 6.77 (d, *J* = 8.79 Hz, 2H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.3, 155.3, 134.6, 131.3, 130.6, 127.5,

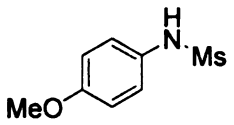
126.9, 121.7, 113.1, 54.6. Physical and spectral data were consistent with commercially available material.



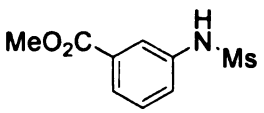
Methyl 3-benzamidobenzoate: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with benzoic anhydride (2 mmol, 0.452 g) afforded 0.2271 g (89%) of methyl 3-benzamidobenzoate as a white solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); mp = 122-123 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.15 (bs, 1H), 8.21 (s, 1H), 7.95 (m, 1H), 7.82 (d, *J* = 7.14 Hz, 2H), 7.66 (d, *J* = 7.69 Hz, 1H), 7.48-7.22 (m, 4H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 166.6, 138.4, 134.3, 132.7, 131.5, 129.5, 128.6, 128.2, 128.0, 127.2, 125.0, 121.4, 51.9; IR (Nujol) 3283, 1724, 1651, 1595, 1529, 1431, 1292, 1226, 1124, 1072, 925, 754, 694 cm^{-1}; LRMS (EI, 70eV) 255 (8), 105 (100), 91 (2), 77 (66); HRMS (EI) *m/z* calcd for $C_{15}H_{13}NO_3$ 255.0895, found 255.0902.



***N*-(2,6-Dimethylphenyl)benzamide**: Subjection of nitro-*m*-xylene (1 mmol, 0.136 mL) to general procedure F with benzoic anhydride (2 mmol, 0.452 g) afforded 0.1327 g (59%) of *N*-(2,6-dimethylphenyl)benzamide as a white solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); mp = 162 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (bs, 1H), 7.83 (d, *J* = 7.14 Hz, 2H), 7.49 (m, 1H), 7.36 (m, 2H), 7.05 (m, 3H), 2.16 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.0, 135.5, 134.1, 133.9, 131.5, 128.4, 128.0, 127.2, 127.1, 18.2. Physical and spectral data were consistent with those previously reported.[166]

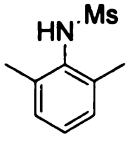


***N*-(4-Methoxyphenyl)methanesulfonamide**: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with methanesulfonic anhydride (2 mmol, 0.348 g) afforded 0.1585 g (79%) of *N*-(4-methoxyphenyl)methanesulfonamide as a pink-purple solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 115 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18 (d, *J* = 8.79 Hz, 2H), 6.96 (bs, 1H), 6.84 (d, *J* = 8.79 Hz, 2H), 3.75 (s, 3H), 2.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.9, 129.1, 124.5, 114.6, 55.4, 38.6; IR (Nujol) 3256, 1512, 1462, 1323, 1284, 1143, 1026, 974, 825, 767 cm^{-1}; LRMS (EI, 70eV) 203 (0.75), 202 (1), 201 (17), 122 (100), 95 (42), 79 (11), 78 (10), 77 (4); HRMS (EI) *m/z* calcd for $C_8H_{11}NO_3S$ 201.0460, found 201.0464.

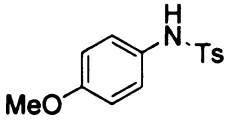


Methyl 3-(methylsulfonamido)benzoate: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with methanesulfonic anhydride (2 mmol, 0.348 g) afforded 0.179 g (78%) of methyl 3-(methylsulfonamido)benzoate as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.95 (bs, 1H), 7.82 (s, 1H), 7.67 (d, *J* = 7.69 Hz, 1H), 7.41 (d, *J* = 7.14 Hz, 1H), 7.28 (t, *J* = 7.69 Hz, 1H), 3.79 (s, 3H), 2.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.3, 137.9, 131.0, 129.3, 125.3, 124.6, 120.9, 52.0, 39.0; IR (Nujol) 3426, 3246, 1718, 1589, 1475, 1437, 1332, 1296, 1155, 1036, 1005, 821, 758 cm^{-1}; LRMS (EI, 70eV) 231 (1), 230 (4), 229 (32), 198 (15), 170 (2), 151 (26), 150 (100), 120 (68), 119 (22), 118 (12), 105 (15), 93 (11), 92 (40), 91 (65), 90 (36), 77 (20), 66 (44), 65 (25),

64 (38), 63 (38), 59 (11) 44 (12); HRMS (EI) *m/z* calcd for $C_9H_{11}NO_4S$ 229.0409, found 229.0409.

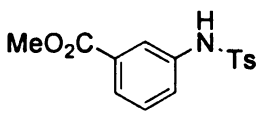


***N*-(2,6-Dimethylphenyl)methanesulfonamide**: Subjection of nitro-*m*-xylene (1 mmol, 0.136 mL) to general procedure F with methanesulfonic anhydride (2 mmol, 0.348 g) afforded 0.0602 g (30%) of *N*-(2,6-dimethylphenyl)methanesulfonamide as a white solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.08 (m, 3H), 6.16 (bs, 1H), 3.05 (s, 3H), 2.39 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.3, 132.7, 128.8, 127.9, 41.7, 19.1; IR (Nujol) 3267, 3011, 1396, 1319, 1147, 983, 900, 769 cm^{-1}; LRMS (EI, 70eV) 201 (0.4), 200 (0.9), 199 (11), 120 (100), 90 (12), 77 (15); HRMS (EI) *m/z* calcd for $C_9H_{13}NO_2S$ 199.0667, found 199.0670.

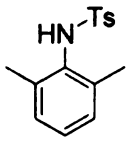


***N*-(4-Methoxyphenyl)-4-methylbenzenesulfonamide**: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with toluenesulfonic anhydride (2 mmol, 0.652 g) afforded 0.2689 g (97%) of *N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 112 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.24 Hz, 2H), 7.20 (s, 1H), 7.14 (d, *J* = 7.69 Hz, 2H), 6.97 (d, *J* = 9.33 Hz, 2H), 6.69 (d, *J* = 8.79 Hz, 2H), 3.68 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6, 143.5, 135.7, 129.4, 129.0, 127.2, 124.9, 114.2, 55.2, 21.4; IR (Nujol) 3267, 3011, 1610, 1597, 1510, 1396, 1332, 1290, 1251, 1219, 1161, 1091, 1030, 912, 812, 679 cm^{-1}; LRMS (EI, 70eV) 277 (9), 122

(100), 91 (20), 77 (3), 64 (20); HRMS (EI) *m/z* calcd for $C_{14}H_{15}NO_3S$ 277.0773, found 277.0768.

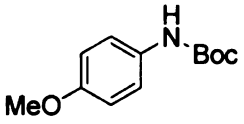


Methyl 3-(4-methylphenylsulfonamido)benzoate: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with toluenesulfonic anhydride (2 mmol, 0.652 g) afforded 0.2982 g (98%) of methyl 3-(4-methylphenylsulfonamido)benzoate as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 152-154 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + d_6-DMSO): δ 9.54 (bs, 1H), 7.65 (s, 1H), 7.54 (d, *J* = 8.24 Hz, 2H), 7.23 (m, 1H), 7.18 (t, *J* = 7.69 Hz, 1H), 7.06 (d, *J* = 8.24 Hz, 2H), 3.72 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + d_6-DMSO): δ 166.4, 143.3, 137.8, 136.3, 130.9, 129.4, 129.0, 127.0, 125.2, 124.8, 121.3, 52.0, 21.3; IR (Nujol) 3227, 1703, 1593, 1477, 1439, 1404, 1336, 1300, 1219, 1159, 1089, 985, 852, 814, 754, 661 cm^{-1}; LRMS (EI, 70eV) 305 (11), 155 (32), 150 (8), 120 (9), 119 (5), 118 (10), 91 (100), 77 (5), 43 (15); HRMS (EI) *m/z* calcd for $C_{15}H_{15}NO_4S$ 305.0722, found 305.0720.

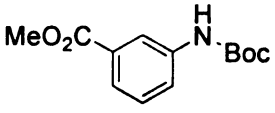


***N*-(2,6-Dimethylphenyl)-4-methylbenzenesulfonamide**: Subjection of nitro-*m*-xylene (1 mmol, 0.136 mL) to general procedure F with toluenesulfonic anhydride (2 mmol, 0.652 g) afforded 0.1994 g (72%) of *N*-(2,6-dimethylphenyl)-4-methylbenzenesulfonamide as a white solid (silica gel FC, hexanes/EtOAc: 95/5, 80/20 then 50/50); mp = 129-131 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.24 Hz, 2H), 7.21 (d, *J* = 8.24 Hz, 2H), 7.05 (m, 1H), 6.99 (m, 2H), 6.32 (bs, 1H), 2.39 (s, 3H), 2.02 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ

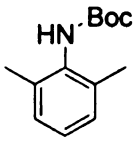
143.5, 137.76, 137.70, 132.5, 129.5, 128.6, 127.6, 127.1, 21.4, 18.6; IR (Nujol) 3271, 1597, 1473, 1369, 1325, 1159, 1091, 898, 817, 781, 673 cm^{-1}; LRMS (EI, 70eV) 275 (9), 120 (100), 91 (31), 77 (16); HRMS (EI) *m/z* calcd for $C_{15}H_{17}NO_2S$ 275.0980, found 275.0982.



***tert*-Butyl 4-methoxyphenylcarbamate**: Subjection of 4-nitroanisole (1 mmol, 0.153 g) to general procedure F with di-*tert*-butyl dicarbonate (2 mmol, 0.436 g) afforded 0.22 g (99%) of *tert*-butyl 4-methoxyphenylcarbamate as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 90-91 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.79 Hz, 2H), 6.79 (d, *J* = 8.79 Hz, 2H), 6.50 (bs, 1H), 3.72 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 153.1, 131.4, 120.5, 114.0, 80.1, 55.3, 28.2. Physical and spectral data were consistent with those previously reported.[167]



Methyl 3-(*tert*-butoxycarbonylamino)benzoate: Subjection of methyl 3-nitrobenzoate (1 mmol, 0.181 g) to general procedure F with di-*tert*-butyl dicarbonate (2 mmol, 0.436 g) afforded 0.056 g (22%) of methyl 3-(*tert*-butoxycarbonylamino)benzoate as a white solid (silica gel FC, hexanes/EtOAc: 80/20 then 50/50); mp = 103 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.65 (m, 2H), 7.32 (m, 1H), 6.71 (bs, 1H), 3.87 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.8, 152.6, 138.6, 130.8, 129.0, 124.0, 122.8, 119.3, 80.8, 52.1, 28.2. Physical and spectral data were consistent with those previously reported.[168]



***tert*-Butyl 2,6-dimethylphenylcarbamate**: Subjection of nitro-*m*-xylene (1 mmol, 0.136 mL) to general procedure F with di-*tert*-butyl dicarbonate (2 mmol, 0.436 g) afforded 0.1105 g (50%) of *tert*-butyl 2,6-dimethylphenylcarbamate as a light yellow oil (silica gel FC, hexanes/EtOAc: 95/5 then 80/20); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.03 (s, 3H), 5.92 (bs, 1H), 2.23 (s, 6H), 1.50 (bs, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.7, 134.0, 127.9, 126.7, 79.7 28.2, 27.3, 18.2; IR (Nujol) 3341, 3003, 1695, 1506, 1248, 1122, 1055, 771 cm^{-1}; LRMS (EI, 70eV) 222 (0.1), 221 (1), 165 (23), 121 (46), 119 (20), 105 (18), 91 (5), 77 (11), 59 (20), 57 (100); HRMS (EI) m/z calcd for $C_{13}H_{19}NO_2$ 221.1416, found 221.1409.

References and Notes

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