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A Synthetic and Mechanistic Investigation into the Cobalt(I) Catalyzed Amination of Aryl Halides

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Employing first-row transition metals in catalytic two-electron transformations remains a synthetic challenge. In order to overcome the common and often deleterious single-electron reactivity, an appropriate strong-field ligand was targeted on cobalt. Herein, we report the Co(I) catalyzed amination of aryl halides with lithium hexamethyldisilazide. This transformation features $(PPh_3)_3CoCl$ (**1**) as the catalyst and affords structurally diverse and electronically varied primary arylamines in good chemical yields, with the scope of the reaction featuring arylamines that cannot be synthesized via traditional metal-catalyzed amination routes, including 4-aminophenylboronic acid pinacol ester. Stoichiometric reactivity revealed that $(PPh_3)_2CoN(SiMe_3)_2$ (**2**) is likely generated within the catalytic cycle and could be independently synthesized from the reaction of $(PPh_3)_3CoCl$ with $LiN(SiMe_3)_2$. Catalytic reactivity featuring the Co-amide complex, $(PPh_3)_2CoN(SiMe_3)_2$, showed that it is a competent catalyst, implying that the $(PPh_3)_3CoCl$ may be serving as a pre-catalyst in the reaction. Both stoichiometric and kinetic studies support the catalytic cycle involving a Co(I) complex. Catalytic reactions featuring Co(II) complexes resulted in undesired biaryl formation, a product that is not observed under standard catalytic conditions and any productive catalytic reactivity likely arises from an in situ reduction of Co(II) to Co(I). A Hammett study was carried out to differentiate between a closed-shell or radical mechanism, the results are consistent with the proposed closed-shell mechanism. Initial studies indicate this reactivity may be expanded to other bulky nucleophiles.

Carbon–nitrogen bonds are abundant in organic molecules and methods for their direct construction in amination reactions from aryl halides are important in small molecule synthesis.[1] The direct synthesis of primary anilines has been carried out using palladium catalysts, ammonia, ammonia surrogates and aryl halides.[2] In carbon–nitrogen bond formation it is often the large substrate scope afforded by the palladium catalysts that is ideal, however the costly metals and ligands necessary to perform these transformations are not. To this end, base metals have become attractive targets in amination reactions mainly mediated by their heavier congeners in part due to the cost and environmental advantage; but more excitingly, due to the potential of these catalysts to facilitate new reactivity.[3] Amination reactions featuring copper catalysts (Ullman coupling) have been studied extensively in the coupling of aryl iodides, and to a lesser extent, aryl bromides with nitrogen nucleophiles; however, the scope of reactivity is limited.[4] Nickel catalyzed amination has been explored.[5] Although cobalt mediated cross-coupling reactions are known,[6] C–N bond coupling is limited to two cobalt(II) catalyzed processes; the first example couples pyridyl-chlorides with piperidine[7] and the second is an intramolecular C–N bond coupling.[8] Both of these methods suffer from dramatically limited substrate scopes compared with the palladium-mediated methods.

The intermolecular amination of unactivated aryl halides with cobalt has, to the best of our knowledge, not been demonstrated, whereas palladium-mediated processes have been quite successful.[2] A key example by Hartwig and co-workers uses a Pd(0) catalyst in the reaction of lithium hexamethyldisilazide ($LiN(SiMe_3)_2$) with aryl halides.[2e-g] In these reactions, $LiN(SiMe_3)_2$ can be cross-coupled with a variety of aryl bromides and chlorides, resulting in the formation of $ArN(SiMe_3)_2$ in good yields. These *N*-aryldisilazides can subsequently be deprotected by acid to yield the primary aniline.[2e-g] *Ortho*-substituted aryl halides failed to react under these conditions, which the authors attribute to the steric properties of the nucleophile.[2e] Subsequently, Buchwald and co-workers confirmed this hypothesis by demonstrating that a less-encumbered primary silylamine, Ph_3SiNH_2, could successfully yield the corresponding *ortho*-substituted aniline following deprotection.[2f] Since coupling α-branched amine nucleophiles is challenging, these reactions were targeted in an effort to evaluate the potential of cobalt-mediated catalysis in C–N cross-coupling reactivity.

Computational work has suggested that the greater density of states for first-row metals should allow for two-electron redox processes, such as oxidative addition, to be more energetically favourable than the analogous reactions with second-row metals.[9] Iron complexes featuring electron rich phosphine ligands have been implicated in both oxidative addition and reductive elimination reactions.[10] More recently, Peters and coworkers reported the oxidative group transfer of a Co(I) molecule, $(PhBP_3)CoPMe_3$ with tolyl azide afforded a cobalt(III)-imido species.[11] Likewise, oxidative addition of H_2 to Co(I) complexes has been observed.[12] Bernskoetter and co-workers concisely demonstrated through deuterium labeling and trapping experiments that $(PMe_3)_3CoI(CH_3)_2$, formed from oxidative addition of methyl iodide to $(PMe_3)_4CoCH_3$, could undergo stoichiometric reductive elimination to yield ethane and an equivalent of $(PMe_3)_3CoI$ via a concerted two-electron process.[13] While the role of the alkyl ligand cannot be discounted, it suggested that a Co(I/III) redox cycle supported by phosphine ligands may be sufficient, under the right conditions, to allow catalysis to occur. Similarly, the Chirik group has recently reported several oxidative addition reactions[12k,14] with a $(PNP)CoCH_3$ complex as well as cobalt-catalyzed C–H borylation.[15] The commonality of all of the described examples is a low-valent, electron rich cobalt(I) center; however, mechanistic studies are necessary to differentiate between the common single electron transfer versus two-electron chemistry by base metal catalysts.

Herein, we present the first cobalt(I)-catalyzed amination of unactivated aryl iodides with $LiN(SiMe_3)_2$ for the formation of various anilines including those not amendable to synthesis through other cross-coupling methods. The reaction is catalyzed by a single-component triphenylphosphine-ligated cobalt(I) precursor. Stoichiometric investigations, trapping experiments and linear free energy studies have been conducted and are inconsistent with single electron transfer featuring a Co(II) intermediate.

Results and Discussion

Optimization of Cobalt-Catalyzed Amination. The cobalt-catalyzed amination of aryl iodides with $LiN(SiMe_3)_2$ was initially investigated. Reaction of one equivalent of iodobenzene with 2.6 equivalents of $LiN(SiMe_3)_2$ in the presence of 7.5 mol% $(PPh_3)_3CoCl$ (**1**) refluxing in toluene for 12 h cleanly resulted in the formation of the *N,N*-bis(trimethylsilyl)aniline in 77% yield, which readily hydrolyzes with acid to aniline. In the absence of **1** no coupling product was observed, suggesting that this is a cobalt-mediated process. The relative importance of solvents, temperature, equivalents of silylamide and ligands on the reaction was evaluated using iodobenzene as a model substrate and the results are listed in Table S1. The choice of solvent was critical for success as coordinating solvents inhibit reactivity (Table S1, entries 1-8). Among the examined solvents, only non-coordinating solvents (toluene (77%), benzene (53%) and hexanes (46%)) gave rise to the coupled amine, with toluene resulting in the highest yield likely due to the increased solubility of the catalyst. Lower temperatures (< 100 °C) did not result in coupled product (Table S1, Entries 34-35).

Since other nucleophiles (e.g lithium amide, lithium diisopropylamide, and lithium ditertbutylamide) did not couple when substituted for $LiN(SiMe_3)_2$, the number of equivalents of $LiN(SiMe_3)_2$ necessary for the transformation was investigated. When only one equivalent of $LiN(SiMe_3)_2$ was utilized, the formation of both aminated product and C–C coupled isomers of methylbiphenyl were observed, from the reaction of an aryl radical with the solvent.[16] The formation of the biaryl product was not detected when 2.6 equivalents of nucleophile was used and increasing nucleophile loading to 5.2 equivalents resulted in formation of aniline in 99% yield.

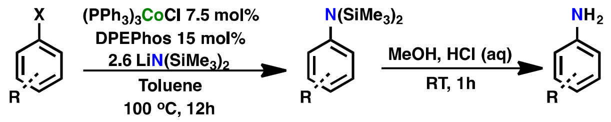
Monitoring the reaction by ^1H NMR at elevated temperature illustrated the loss of PPh_3 under the reaction conditions, suggesting that the addition of an electron rich bidentate phosphine ligand may improve overall catalysis. The addition of a variety of chelating phosphine ligands (15 mol%) to **1** resulted in the formation of aniline in higher yields (DPPF (97%), BINAP (99%) and DPEPhos (95%), Table S1, entries 11-14). The addition of DPPE, however, resulted in lower yield (68%) than any of the other phosphines. DPEPhos was chosen as the added phosphine on the basis of improved yield and overall cost effectiveness. The reaction conditions were optimized on the basis of these results to include 2.6 equivalents of nucleophile, 15 mol% of DPEPhos, and 7.5mol% of **1** at 100 °C in toluene. Lowering the catalyst loading from 7.5 mol% to 4 mol% and 2 mol% resulted in reduced product yields.

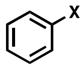
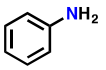
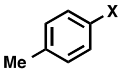
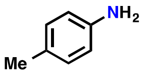
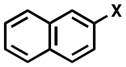
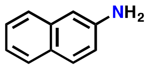
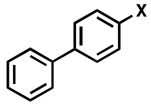
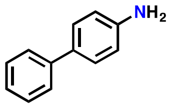
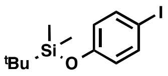
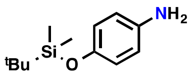
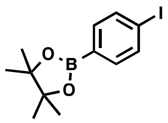
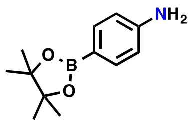
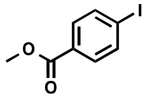
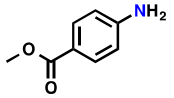
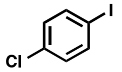
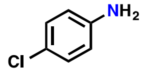
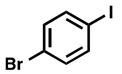
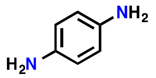
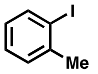
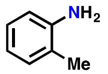
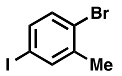
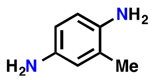
Substrate Scope. With the optimized reaction conditions in hand, the scope of substrates was explored (Table 1). Under the optimized conditions, aryl iodides are the most reactive substrates; aryl bromides such as bromobenzene, 4-bromobiphenyl, and 2-bromonapthalene furnish the aminated product in good yield, albeit diminished relative to the analogous aryl iodides. Aryl chlorides, however, are unreactive under the reaction conditions, even for prolonged reaction times. Although aryl triflates typically tend to result in similar two-electron chemistry as aryl iodides; the reactivity observed led to an intractable mixture of organic products. The reaction of aryl iodides featuring electron-donating groups (Me, Ph, napthyl and OTBS) furnished the aminated product in excellent yields (entries 2-5) while electron-withdrawing groups were also tolerated in decent yields (entries 7-9).

The scope of this cobalt-catalyzed reaction tolerates several notable substrates not amenable to the existing Pd-mediated methods. For example, a boronate ester is tolerated under the reaction conditions to afford 4-aminophenylboronic acid pinacol ester in excellent yield (91%); palladium-catalyzed methods require installation of the amine prior to the boronate functionality.[17] In a second example, use of 4-chloroiodobenzene as a substrate resulted in the formation of *p*-chloroaniline, leaving the chloride as a functional group handle for further elaboration by other cross-coupling methods. Conversely, the reaction with 4-bromoiodobenzene resulted in the formation of *p*-phenylenediamine (entry 9) in 94% yield after acidic workup.

Although this cross-coupling reaction can tolerate *ortho*-substitution (entry 10), the yields are diminished dramatically with respect to the *meta*- and *para*-substituted counterparts. Previously reported palladium-catalyzed reactions failed in the case of *ortho*-substituted aryl halides and bis(trimethylsilyl)amide likely due to the significant bulk of the two trimethylsilyl groups.[2g] Interestingly, when 2-bromo-5-iodotoluene is used as a substrate, 2,5-

Table 1. Substrate Scope.



Entry	Aryl Halide	GC Yield of $RPhN(SiMe_3)_2$	Product	Isolated Yield
1		X = I 95% X = Br 65% X = Cl No RXN		X = I 91% X = Br 60%
2		X = I 99% X = Br 69%		X = I 96% X = Br 61%
3		X = I 99% X = Br 69%		X = I 94% X = Br 63%
4		X = I 77% X = Br 45%		X = I 74% X = Br 39%
5		99%		90%
6		96%		91%
7		64%		58%
8		73%		70%
9		99%		94%
10		37%		30 %
11		77%		69 %

Conditions: Aryl halide (1 mmol), $LiN(SiMe_3)_2$ (2.6 mmol), **1** (0.075 mmol), DPEPhos (0.15 mmol), toluene (5 mL) 100˚C, 12 h. Yields reported as the average of three runs.

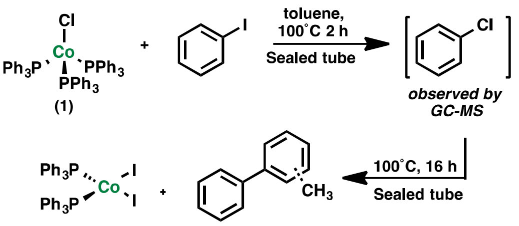
diaminotoluene could be isolated in 74% yield, indicating that the addition of the electron-donating group resulting from the first coupling enhanced the reactivity, ultimately overcoming the steric constraints of the *o*-methyl (entry 11).

Mechanistic Considerations. Based on the previously established literature precedent of **1** to participate in radical chemistry[6] we sought to understand this catalytic process in more detail to delineate a two-electron pathway and a radical or caged radical mechanism. As such, both stoichiometric and catalytic reactions were explored with iodobenzene as the model substrate. In palladium coupling, benzyne intermediates have been proposed, and the lower yields observed by electron deficient substrates are consistent with this mechanistic pathway. However, the expected regioisomers from benzyne formation are never observed in our reaction.[2e,18] Furthermore, replacing toluene with durene as the solvent in the catalytic transformation did not result in formation of the Diels-Alder adduct, which has been shown to trap the putative benzyne intermediate.[19] Similarly, in a recently reported Ullman coupling, C–N bond formation in carbazole proceeds via a photo-induced single electron transfer.[20] To determine whether the observed coupling proceeds through a photoinduced aminyl radical generated from $LiN(SiMe_3)_2$, the reaction was conducted in the absence of light under standard catalytic conditions. Running the reaction in the dark did not diminish the yield of aniline formation (96%) (Table S1, entry 16).

To investigate the possibility of radical intermediates during catalysis, various radical traps were employed including 1,4-cyclohexadiene, BHT (2,6-di-*tert*-butyl-4-methylphenol) and 1,1-diphenylethene. Under standard catalytic conditions the primary aryl amine was solely formed and the unconsumed additive was detected by GC-MS. Mechanistic studies of the elimination of ethane from $(PMe_3)_3Co(CH_3)_2I$ by Bernskoetter and coworkers suggested that these results are evidence against an uncaged radical intermediate; however, a caged radical could be present.[13] Addition of other radical traps such as TEMPO and $ClCPh_3$, not surprisingly, reacted with **1** or the nucleophile prior to being exposed to the catalytic conditions, resulting in a myriad of products.

Stoichiometric Reactivity. In order to assess the role of single- versus two-electron transfer reactions, we sought to develop an understanding of the behavior of **1** in a stoichiometric regime. As depicted in Scheme 1, exposure of **1** to one equivalent of iodobenzene at room temperature in toluene did not result in a reaction as determined by GC-MS or ^1H NMR spectroscopy. Monitoring the heated mixture (100ºC) by GC-MS resulted in quantitative conversion of the iodobenzene to chlorobenzene in the first four hours of the reaction. Additional heating (12 h) converted the chlorobenzene quantitatively to biaryl. The organic products were then removed by extraction with toluene, from which $(PPh_3)_2CoI_2$ was isolated.[21] The ratio of biaryl isomers observed is consistent with that reported in the radical reaction with the solvent (o: m: p = 1.6: 1.0: 2.0).[16a]

Stoichiometric reactions between **1** and iodobenzene were also conducted in the presence of $LiN(SiMe_3)_2$. If **1** and iodobenzene are stirred together at 100ºC as previously described before the addition of $LiN(SiMe_3)_2$, the only product obtained after 12 hours is a mixture of biaryls. However, when $LiN(SiMe_3)_2$ is added before the reaction is heated, the aminated product is isolated in 70% yield; the same result is obtained when **1** and $LiN(SiMe_3)_2$ are stirred at 100ºC prior to the addition of iodobenzene. Chlorobenzene is not observed

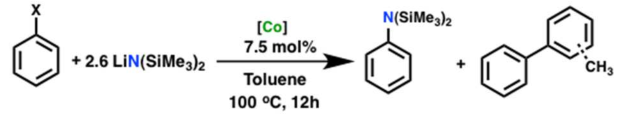


Scheme 1. Stoichiometric reaction of **1** with iodobenzene.

in any reaction in which the nucleophile is added before or concurrently with iodobenzene. These results suggest that a non-productive halide metathesis can occur between the cobalt complex and iodobenzene, irreversibly converting the reactive aryl iodide into an inert aryl chloride, which then may be consumed by a Co(II) species arising from the known disproportionation pathway of the unstable $(PPh_3)_2CoI$.[22] The presence of nucleophile prevents this equilibration and results in the formation of the desired arylamine product.

Cobalt(II) as an intermediate. Although evidence for radical formation was not detected with various radical trapping experiments (*vide supra*), the potential for the formation of a Co(II) intermediate within the catalytic cycle is plausible. In this regard, $(DPEPhos)CoCl_2$ was substituted for **1** in the catalytic reaction. Surprisingly, the reaction formed both the desired arylamine product and biaryl isomers in a 1:1 mixture (Table 2). This is in stark contrast to the reaction with **1**, which forms only arylamine under standard catalytic conditions. Furthermore, $(DPEPhos)Co(N(SiMe_3)_2)_2$ was prepared[23] *in situ* from the reaction of two equivalents of DPEPhos with $Co_2(N(SiMe_3)_2)_4$ and submitted to the reaction conditions, yielding an 85:15 mixture of arylamine and biaryl isomers. Increasing the amount of $(DPEPhos)Co(N(SiMe_3)_2)_2$ to 15 mol% complex increased the ratio of arylamine to biaryls (70:30).

Table 2. Divergent reactivity of Co(I) and Co(II).



Entry	X	[Co]	Aniline	Biaryl
1	I	$(PPh_3)_3CoCl$ (1)	77%	0%
2	I	$(DPEPhos)CoCl_2$	50%	50%
3	I	$(DPEPhos)Co(N(SiMe_3)_2)_2$	85%	15%
4	Cl	$(PPh_3)_3CoCl$ (1)	0%	0%
5	Cl	$(DPEPhos)CoCl_2$	0%	95%
6	Cl	$(DPEPhos)Co(N(SiMe_3)_2$	0%	98%
7	I	$(PPh_3)_3CoCl$ (1) + Zn	65%	0%
8	I	$(DPEPhos)CoCl_2$ + Zn	68%	0%
9	I	$(DPEPhos)Co(N(SiMe_3)_2)_2$ + Zn	69%	0%
10	Cl	$(PPh_3)_3CoCl$ (1) + Zn	0%	0%
11	Cl	$(DPEPhos)CoCl_2$ + Zn	0%	0%
12	Cl	$(DPEPhos)Co(N(SiMe_3)_2)_2$ + Zn	0%	0%

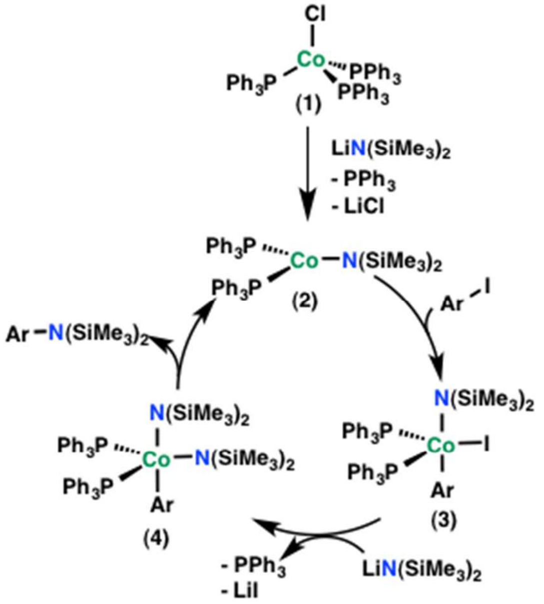
Given the distinct reactivity of **1** and the cobalt(II) catalysts, we sought to reconcile the role of each. As previously described, **1** did not react with chlorobenzene under the standard reaction conditions and offered an opportunity to understand the divergent reactivity profiles of the two oxidation states. As described in Table 2, the reactions of $(DPEPhos)CoCl_2$ or $(DPEPhos)Co(N(SiMe_3)_2)_2$ with chlorobenzene as a substrate differentiate themselves from the reactions of both Co(I) and Co(II) with iodobenzene. While $(DPEPhos)CoCl_2$ and $(DPEPhos)Co(N(SiMe_3)_2)_2$ form arylamine from iodobenzene, the sole isolated product from the reaction with chlorobenzene is biaryl isomers, suggesting that a Co(II) species is likely responsible for the formation of biaryl byproduct. If a Co(II) species was accessed in our catalytic cycle, then reacting **1** (under standard conditions) with a 50:50 mixture of iodo- and chlorobenzene should result in the isolation of biaryl products. Instead these reaction conditions resulted in no biaryl products and a mixture of 50% of aniline and unconsumed chlorobenzene (50% via GC-MS).

To understand this reaction further, zinc metal was added to several reaction mixtures as described in Table 2. The addition of a reductant to standard catalytic conditions with **1** as the catalyst should have no effect on catalysis if a cobalt(I) species is necessary. However, if under catalytic conditions the Co(I) species is oxidized to Co(II) and that is the productive catalyst, then catalysis should be inhibited. Zinc metal has not been shown to be a strong enough reductant to access Co(0).[24] The addition of zinc (Table 2, Entry 7) resulted in a slightly decreased yield of the desired aniline product, but no biaryl species were formed (the diminished yield is possibly due to the heterogeneity of the reaction mixture under these conditions; a similar decrease in yield is observed when the reaction is run without stirring).

If Co(I) is the active species, the addition of zinc to the reaction mixture should produce arylamine exclusively, regardless of whether the starting complex is Co(I) or Co(II) due to *in situ* reduction of Co(II) species present in the reaction mixture. Conversely, if arylamine is not observed under these conditions, it may speak to the involvement of a Co(II) intermediate in the catalytic cycle. Gratifyingly, when either $(DPEPhos)CoCl_2$ or $(DPEPhos)Co(N(SiMe_3)_2)_2$ are submitted to the standard catalytic conditions in the presence of Zn, desired aniline product is the sole isolated product in 68% yield. These results are consistent with reduction of the Co(II) species to Co(I). To test this hypothesis further, replacing iodobenzene with chlorobenzene under standard catalytic conditions should result in no reaction, since chlorobenzene is not a productive substrate for the amination reaction. As listed in Table 2, Entries 11-12, no aniline or biaryl was detected and chlorobenzene could be reisolated from the reaction mixture.

Catalytic Cycle. The previously described stoichiometric and catalytic studies support Co(I) as the active catalyst. Based on these results the following Co(I)/Co(III) catalytic cycle is proposed (Scheme 2). Compound **1** initially reacts with an equivalent of

Scheme 2. Proposed Catalytic Cycle.



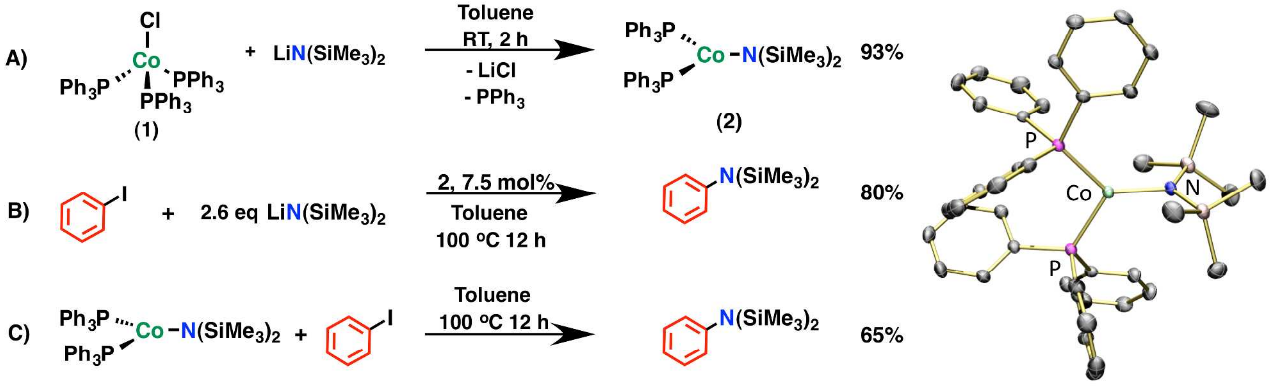


Figure 1. Synthesis (A) and reactivity (B and C) of **2**. Solid state structure of $(PPh_3)_2CoN(SiMe_3)_2$ **(2)** with thermal ellipsoids drawn at 50% (right). Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (°): Co–N 1.918(2), Co–P 2.2545(9) and 2.2425(9); P–Co–N 129.51(8) and 123.78(8), P–Co–P 106.35(3).

$LiN(SiMe_3)_2$ to produce a new Co(I) species, $(PPh_3)_2CoN(SiMe_3)_2$ (**2**) which is proposed to be the active catalyst. Next, oxidative addition of the aryl halide results in the formation of a Co(III) species, $(PPh_3)_2CoPhI(N(SiMe_3)_2$ (**3**). Given the need for multiple equivalents of nucleophile, this species likely undergoes a second substitution with nucleophile prior to reductive elimination of product. Based on the proposed cycle, we sought several avenues to isolate intermediates within the proposed catalytic cycle.

The amide species, $(PPh_3)_2Co(N(SiMe_3)_2)$ (**2**) can be isolated in 93% yield from a reaction between $(PPh_3)_3CoCl$ and $LiN(SiMe_3)_2$ in toluene at room temperature (Figure 2A).[25] X-ray quality crystals of **2** were grown from a cold concentrated solution of Et_2O (Figure 1). Compound **2** displays a three-coordinate Co(I) ion in a trigonal planar geometry with P–Co–N bond angles of 129.51(8)° and 123.78(8)° and a Co–N distance of 1.918(2) Å. Importantly, this complex is both catalytically (Figure 1B) and stoichiometrically competent (Figure 1C) for the formation of product in yields mildly better than that of **1**. This suggests that **1** may function as a pre-catalyst, whereby initial reaction with $LiN(SiMe_3)_2$ yields the catalytically active species, **2**.

Efforts to isolate a Co(III) species from reaction of **2** with aryl halides were hindered by the reactivity of the products; at the temperatures required for a productive reaction to occur, all intermediates proceeded to arylamine before a complex could be isolated. The increased yield upon addition of a bidentate phosphine is consistent with reductive elimination from the five-coordinate species, **4**. Additional equivalents of triphenylphosphine or DPEPhos did not hamper the overall reaction. Furthermore, monitoring a catalytic reaction by ^{19}F NMR spectroscopy of the addition of excess tris(4-fluorophenyl)phosphine did not result in a new ^{19}F NMR signals. Dissociation of a phosphine ligand is not likey and reductive elimination to the three-coordinate species, **2**, is not rate determining.

Hammett Study. Given the difficulty in isolating a Co(III) intermediate, a Hammett study was performed to differentiate between closed-shell or radical mechanisms by comparing the fits of σ and $\sigma^{\bullet}$ values,[26] respectively, as previously demonstrated by Norrby and co-workers as well as others.[27] Since the correlation parameters and ρ values for oxidative addition and reductive elimination are known from stoichiometric studies with palladium complexes,[28] the substituent effect on the relative rate of the reaction is a powerful tool for understanding this cobalt-mediated amination reaction.

The six competition reactions between unsubstituted and various *para*-substituted iodobenzenes were monitored by GC using the appearance of products versus an internal standard of mesitylene. To simplify the reaction set-up and analysis, the reaction was run without DPEPhos; instead 5.2 equivalents of $LiN(SiMe_3)_2$ were employed. We propose that the reaction order is the same for all substrates studied; under this assumption, the k_{rel} values could be obtained in a manner previously described (see Equation S1 for more details).[27] The kinetic studies all yielded straight lines ($r^2 > 0.96$, Figure S1).

The relative rates and different σ values used for the Hammett plot are listed in Tables S2 and S3, respectively. Figure 2 depicts the plot of $\log(k_{rel})$ vs. $\sigma^{\bullet}$ values (depicted by ♦ marks) or σ values (depicted by ■ marks). Regardless of which open-shell parameter, $\sigma^{\bullet}$, is used, total scatter is obtained ($\sigma^{\bullet}$ values described by Jiang[26d] are depicted in Figure 4, others in Figure S3). The poor fit of the $\sigma^{\bullet}$ values is inconsistent with a single-electron or radical mechanism. The resulting concave plot for the best fit of standard closed-shell σ constants ($r^2 = 0.96$ for $\sigma < 0$ and 0.98 for $\sigma > 0$) is in good agreement with the catalytic coupling of $LiN(SiMe_3)_2$ and aryl halides proceeding via a closed-shell mechanism.

The existence of two lines in the Hammett correlation fitted with σ values suggests that a change in mechanism or a change in the transition state occurs when more electron deficient substrates are used. The line consisting of the *para*-methoxy-, methyl-, and phenyl-substituted substrates ($\sigma < 0$) yields a ρ value of -1.63, indicative of a build-up of positive charge in the transition state. This result is consistent with an oxidative addition-type mechanism, whereby a late, largely polarized transition state, is stabilized by inductive donation from the substrate. The line made up of the *para*-fluoro-, chloro-, and trifluoromethyl-substituted substrates ($\sigma > 0$) yields a ρ

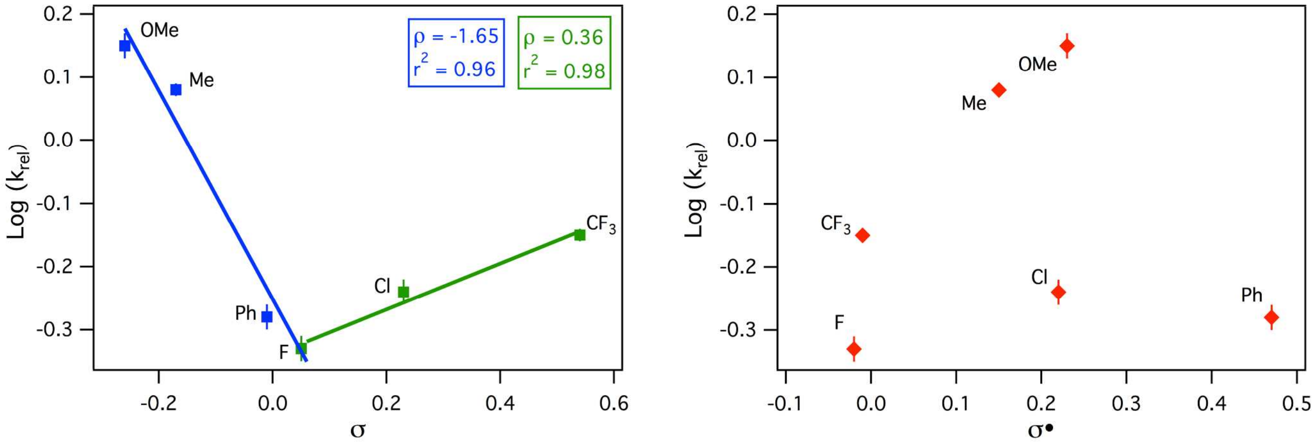


Figure 2. Hammett correlation diagrams. On left, Hammett plot of log(k_{rel}) vs. σ (closed-shell); on right, Hammett plot of log(k_{rel}) vs. $\sigma^{\bullet}$ (Jiang, open-shell). Plots of other σ values can be found in the Supporting Information. The relative rate constants, k_{rel}, are calculated using a plot of $\ln([X_0]/[X]) = k_{rel}*\ln([H_0]/[H])$, where X_0 and H_0 refer to the initial concentrations of functionalized and unfunctionalized iodoarenes, respectively.

value of 0.33, indicating a build-up of negative charge in the transition state. Consequently, this can be characterized as a reductive elimination mechanism, wherein the small ρ value suggests an earlier, less polar transition state. These results are in agreement with similar studies carried out on stoichiometric oxidative addition and reductive elimination reactions with palladium.[28] Unlike palladium, however, the reductive elimination pathway observed with cobalt appears to be less sensitive to electronic effects, suggesting that the η^2-arene complex often invoked for the reductive elimination of C–X bonds from arylpalladium amido complexes[28] does not form with cobalt. It is worth noting that, despite the change in mechanism, the relative rates for electron deficient substrates are lower than those for the electron rich substrates, and may suggest that the poorer yields observed for those substrates are a result of their difficulty in reductively eliminating the arylamine product.

Alternative Nucleophiles. Another important conclusion that can be drawn from the shape of the plot in Figure 4 is that at least one intermediate connects starting material to product in a stepwise mechanism, rather than a concerted process, such as σ–bond methathesis. A corollary of this observation is that such an intermediate might be intercepted by nucleophiles other than $LiN(SiMe_3)_2$. Unfortunately, attempts to cross-couple other nucleophiles, such as arylmagnesium halides and even other lithium amides, using **1** as a catalyst were unsuccessful.

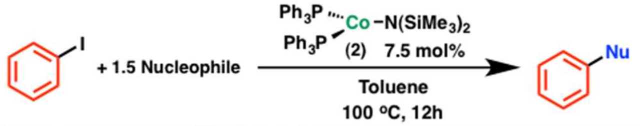
However, the coupling of lithium piperidide with iodobenzene could be accomplished, albeit in very low yields (12%), when $LiN(SiMe_3)_2$ was also present in the reaction mixture (Table S1, Entry 42). Importantly, no cross-coupling of $LiN(SiMe_3)_2$ to form N,N-bis(trimethylsilyl)aniline was observed under these conditions. Given that $(PPh_3)_2CoN(SiMe_3)_2$ is the likely resting state of the catalyst, this suggested that the role of $LiN(SiMe_3)_2$ in the reaction may also be as a spectator ligand increasing the electron richness of the metal center. Under such an assumption, the initial substitution of the cobalt(I) chloride proceeds to yield $(PPh_3)_2CoN(SiMe_3)_2$, which then undergoes oxidative addition to yield an intermediate poised to react with another equivalent of nucleophile. Reductive elimination from this intermediate may furnish multiple products resulting from reaction with the incoming nucleophile, as well as $LiN(SiMe_3)_2$.

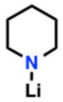
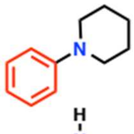
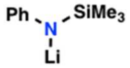
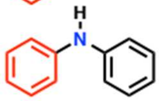
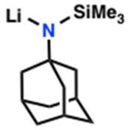
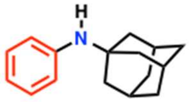
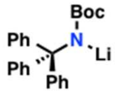
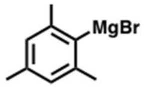
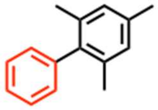
To test this hypothesis, **2** was used as the catalyst for the cross-coupling of other nucleophiles. Complex **2** was initially used as the catalyst to ensure that the stoichiometry and association of $N(SiMe_3)_2$ to the metal was exactly 1:1. The reaction of lithium piperidine and iodobenzene with **2** as the catalyst (Table 3, entry 1) was accomplished in moderately better yields than with **1**. After 12 hours, unreacted iodobenzene was present but increased reactions times did not improve the overall yield. Gratifyingly, lithium *N*-trimethylsilylaniline, generated *in situ* from the parent amine and butyllithium, and mesitylmagnesium bromide cross-coupled cleanly and selectively under the standard reaction conditions with **2** as the catalyst (Table 3, Entry 6). Furthermore, protected alkylamines, including those bearing bulky α–substituents, cross-coupled in good to excellent yields (Table 3, Entries 3-5). This result is intriguing since comparable palladium-mediated methods suffer from severe limitations in cross-coupling bulky alkylamines, suggesting that further optimization of this method may simplify the synthesis of highly encumbered arylamines. Already, the cross-coupling of *tert*-butyltritylcarbamate (Table 3, Entry 5) represents the only reported example of cross-coupling involving a tritylamine synthon. The bis(trimethylsilyl)amide ligand is essential in the coupling of these bulkier nucleophiles and the investigation into its role is currently underway in our laboratories in addition to the expansion of this reaction scope.

Conclusions

The identification of a model complex through which cobalt-mediated two-electron redox catalysis could be studied has been presented, providing a key entry into the library of first row transition metal complexes capable of two-electron catalytic transformations. Both stoichiometric and kinetic studies support the assignment of a closed-shell mechanism for the catalytic amination of aryl halides with $(PPh_3)_3CoCl$ as the catalyst. Reactions with various trapping agents disfavored mechanisms invoking uncaged radicals or aryne intermediates. Differentiating between a caged radical intermediate and a two-electron pathway was less straightforward, and was investigated in two ways. Stoichiometric reactivity was examined by assessing the reactivity of Co(II) intermediates. In these cases, the product distributions included biaryl side products, which arise from a known radical pathway.

Table 3. Coupling of Alternative Nucleophiles with **2**.



Entry	Nucleophile	Product	Isolated Yield[a]
1			20%
2			15%[a]
3			93%
4			45%[a]
5			58%
6			31%

Conditions: Iodobenzene (1 mmol), Nucleophile (4.5 mmol), **2** (0.075 mmol), toluene (5 mL) 100˚C, 12 h. Yields reported as the average of three runs.
[a]Deprotected with 1N HCl prior to isolation.

Any productive catalytic reactivity likely arises from *in situ* reduction of a Co(II) intermediate to Co(I). The addition of a reductant such as Zn prevented the formation of biaryl, implying that a Co(II) intermediate is unlikely to be operative in the amination reaction. Additional support for this came via a Hammett study, which clearly correlates a multi-step, closed-shell mechanism. While work is still ongoing to isolate the key Co(III) intermediate, the collection of results support a closed-shell mechanism catalyzed by a Co(I) species. In conclusion, this work demonstrates the first example of cobalt-mediated intermolecular amination of unactivated aryl halides.

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Notes and references

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Electronic Supplementary Information (ESI) available: Full experimental, crystallographic and spectroscopic data. CCDC See DOI: 10.1039/b000000x/

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