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Hydrodehalogenation of Aryl Chlorides and Aryl Bromides Using a Microwave-Assisted, Copper-Catalyzed Concurrent Tandem Catalysis Methodology

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Supporting Information

ABSTRACT: A concurrent tandem catalytic methodology has been developed for the hydrodehalogenation of aryl bromides and aryl chlorides. The first step of the tandem catalytic cycle, halogen exchange, produced yields of 84-97% from aryl bromides using 5 mol % CuI catalyst, 10 mol % *N*,*N'*-dimethylcyclohexane-1,2-diamine (1), and 2 equiv of NaI in acetonitrile under microwave radiation at 100 °C in 0.5–1.5 h. The same reaction for aryl chlorides appeared to be equilibrium-limited after 1 hour at 200 °C (yields of 5-44%). Both aryl bromides and aryl chlorides were hydrodehalogenated in 12-87% yield



using 20 mol % CuI, 1.5 equiv of diamine 1, and 2 equiv of NaI in acetonitrile at 200 °C after 1-2 h. Substrates with oxygen- or nitrogen-containing functional groups had substantially lower yields than hydrocarbon substrates. Deuterium labeling studies suggest that diamine 1 supplies the majority of the hydrogen for the hydrodehalogenation reaction, but solvent can also serve as a source.

■ INTRODUCTION

Concurrent tandem catalysis (CTC) is an area of synthetic chemistry in an early stage of development. As described by Baker and Bazan,¹ CTC is defined as a transformation in which two or more catalytic cycles operate in a cooperative manner in a single reactor. An example is shown in Scheme 1 in which substrate **A** is transformed by catalyst I into intermediate **B**, which then enters a second catalytic cycle operated by catalyst II to give product **P**. The advantages of CTC lie in the ability to avoid losses in time and yield involved with isolating intermediates in a multistep reaction sequence. However, the challenges in developing successful CTC cycles include compatibility of catalysts with solvent, substrates, products, and each other, as well as reaction sequence selectivity.

In their review of CTC, Baker and Bazan state, "efficient catalysts may allow the coupling of equilibrium-limited reactions with subsequent exothermic ones."¹ As applied to Scheme 1, this situation would correspond to the case where **A** and **B** are in equilibrium mediated by catalyst I, an equilibrium that need not favor **B**, but the subsequent high-yielding reaction of **B** to produce product **P** mediated by catalyst II would result in an overall efficient conversion of **A** to **P**. We describe in this article the development of exactly such a CTC cycle as applied to one of the most widely used classes of substrates, aryl halides.

Aryl halides are useful compounds with important applications in chemical synthesis, particularly as substrates in transition metal-catalyzed coupling reactions to form new carbon—carbon and carbon—nitrogen bonds. Aryl halides are commonly used substrates for the Heck, Suzuki, Stille, Negishi, Kumada, Scheme 1. Concurrent Tandem Catalytic (CTC) Cycle^a





Buchwald-Hartwig, and other coupling reactions. The ratedetermining step in these transformations is often the activation of the strong C-halogen bond.² The strength of the C-halogen bond in these compounds typically follows the trend C-F > $C-Cl > C-Br > C-I;^{3}$ in general, aryl chlorides are much less reactive than the corresponding aryl iodides. Therefore, aryl iodides are more desirable starting materials for coupling reactions but have a limited commercial availability as compared to aryl chlorides or aryl bromides. The greater reactivity of C-I bonds over C-Cl and C-Br bonds can be exploited by developing a general CTC cycle that first converts an aryl chloride or bromide to an aryl iodide in a pre-equilibrium step prior to a second, high-yielding synthetic transformation that occurs in the same reactor (Scheme 2). In the first step (reaction A using catalyst I), an aryl chloride or aryl bromide undergoes halide exchange in the presence of a metal catalyst and a source of iodide to produce a more reactive aryl iodide substrate. This initial reaction may be equilibrium-limited in the absence of a second

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catalytic cycle, but the equilibrium will continue to consume aryl chloride or aryl bromide as the newly formed aryl iodide then serves as the substrate in the subsequent second reaction (reaction B using catalyst II) to form the desired product. An advantage of this approach is that the methodology can be generalized by varying the identity of reaction B. For example, if reaction B were a C–C or C–N bond forming reaction, the





 Table 1. Microwave-Assisted Copper-Catalyzed Halide Exchange of Aryl Bromides to Form Aryl Iodides



^{*a*} Isolated yields (average of two runs); \geq 95% purity as determined by GC; all reactions proceeded to >99% conversion of aryl bromide. ^{*b*} GC yield. ^{*c*} Performed at *T* = 150 °C. successful development of the tandem catalysis process proposed in Scheme 2 would allow for efficient use of commercially available aryl chlorides as substrates in such coupling reactions. Currently aryl chlorides are viable starting materials typically with catalysts that use highly electron-rich and sterically bulky phosphine ligands,^{4–9} but these ligands can be air-sensitive and expensive.

We began development of the CTC methodology outlined above by identifying an appropriate halogen exchange reaction (reaction A). In 2002, Buchwald reported a highly efficient copper-catalyzed aromatic Finkelstein reaction for aryl bromides.¹⁰ Given the long reaction times required under Buchwald's conditions, we first sought to further improve the process by developing this first step in the tandem catalysis pathway to take place under microwave conditions. Reactions performed in a microwave reactor often benefit from a decrease in reaction times (from hours to minutes), a reduction in side-product formation, and an overall improvement in yield and reproducibility.^{11,12} There is also ample literature precedence for tandem catalysis to occur with microwave assistance.^{13–30} Reports of microwave-assisted Heck coupling,^{28,31–36} Buchwald—Hartwig amination,^{33,37–40} Sonogashira coupling,^{33,41–55} Suzuki coupling,^{33,56–60} and hydrodehalogenation,^{61,62} all desirable choices for reaction B in our tandem catalysis process, have been published.

A survey of the literature revealed four previous examples of CTC cycles involving halide exchange of aryl halides as reaction A. Two of the studies focused on aryl chloride to aryl iodide conversion followed by either Sonogashira⁶³ or Heck couplings⁶⁴ with modest yields (18–85%) of product reported. The two other studies by Buchwald⁶⁵ and Wang^{66–68} started with the more reactive aryl bromides or highly activated aryl chlorides followed by cyanation, resulting in modest to good yields.

RESULTS AND DISCUSSION

Adaptation of Buchwald's halogen exchange reaction for the conversion of aryl bromides into aryl iodides to microwave





^{*a*} GC yields (average of two runs).

conditions was achieved using 5 mol % CuI, 10 mol % racemic *trans-N,N'*-dimethylcyclohexane-1,2-diamine (1), and 2 equiv of NaI in acetonitrile at 100 °C. As shown in Table 1, aryl iodides were isolated in good to excellent yields (84-97%) after reaction times of 30-120 min, much shorter than the 22-24 h reported using thermal heating. Compared to thermal heating, the tolerance of the reaction to steric hindrance (entry 4) and the presence of various functional groups (entries 5-8) under microwave conditions remained unchanged.

In contrast, the analogous halogen exchange of aryl chlorides under microwave heating at 200 °C for 1 h (Table 2) produced aryl iodides in only 5–44% yield. Yields were not improved by changing the reaction temperature, lengthening the reaction time, or increasing the amount of NaI added. The lack of efficient conversion of aryl chlorides to aryl iodides is evidence of the equilibrium-limited nature of halogen exchange, where the position of the equilibrium is largely determined by the solubility difference of the two halide salts.¹⁰ However, such poor yields of aryl iodides did not prevent the successful usage of aryl chlorides as starting materials in the CTC method shown in Scheme 2.

Hydrodehalogenation was chosen as the second reaction in our initial investigation of the CTC methodology (Scheme 3, reaction B) since small amounts of arene were observed in some of the product mixtures derived from the halogen exchange of aryl bromides to form aryl iodides. These results suggested that the same catalyst/ligand system responsible for halogen exchange could also perform hydrodehalogenation. The use of the same catalyst/ligand system for both steps in the CTC

Scheme 3. CTC Cycle Composed of Halogen Exchange of Aryl Bromide or Aryl Chloride Followed by Hydrodehalogenation



Table 3. Screening Conditions for Hydrodehalogenation of 4-Chlorotoluene



entry	mol % CuI	<i>T</i> (°C)	ligand	equiv ligand	equiv NaI	time (h)	% conv ArCl ^a	% yield toluene ^b
1	20	200	1	1.5	2	2	95	80
2	20	200	2	1.5	2	1	71	19
3	20	180	1	1.5	2	2	94	61
4	20	200	1	1.5	2	1	94	70
5	20	200	1	0.4	2	1	65	24
6	20	200	1	3.0	2	1	95	68
7	10	200	1	1.5	2	1	85	33
8	20	200	1	1.5	1	1	92	55 ^c
9	20	200	1	1.5	0	2	35	21 ^c
10	20^d	200	1	1.5	0	2	12	3

^{*a*} Determined by GC. ^{*b*} GC yield versus standard (*n*-decane). ^{*c*} According to GC, approximately 14 mol % of the substrate is converted to unobserved/ unidentified side products. ^{*d*} CuCN used as copper source.

methodology would be advantageous since this would circumvent one of the challenges of CTC, the compatibility of the catalysts and ligands of the two catalytic cycles with each other, any reagents, and both sets of substrates and products. Hydrodehalogenation of aryl bromides and aryl chlorides is a methodology of interest since many aromatic halides are carcinogenic, resistant to biodegradation, and harmful to the environment.³ For example, polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), brominated flame retardants, and chlorinated dioxins have been linked to a variety of health problems, such as birth defects and cancer.^{3,69} Hydrodechlorination involving copper has previously been seen in Cu(I)-*n*butylamine catalyst systems.⁷⁰ Hartwig also observed some hydrodeiodination in the Cu(I)-phenanthroline-mediated etherification of sterically hindered aryl iodides.⁷¹

The conditions screened for optimizing the microwave-assisted CTC hydrodehalogenation method using 4-chlorotoluene as the substrate are shown in Table 3. The highest conversion of aryl chloride (95%) and highest yield of toluene (80%) were obtained using 20 mol % CuI, 1.5 equiv of ligand 1, and 2 equiv of NaI in acetonitrile at 200 °C after heating for two hours (entry 1); the 15% of 4-chlorotoluene not converted to toluene was accounted for as 4-iodotoluene. In comparison, when the reaction was performed with 1.5 equiv of less expensive diamine ligand 2 (entry 2), toluene was produced in only 19% yield. Decreasing the temperature to 180 °C (entry 3) decreased the product yield by nearly 20% due to unreacted 4-iodotoluene. Decreasing the reaction time to 1 h (entry 4) led to the synthesis of toluene in 70% yield. By comparing entry 4 to entries 5-8, one can see the effect of varying other reaction parameters. Decreasing the amount of ligand 1 to 40 mol % (entry 5) resulted in a noticeable decrease in both percent conversion of aryl chloride and yield of product; a similar effect was seen when catalyst loading was decreased to 10 mol % (entry 7). Increasing the amount of 1 to 3 equiv (entry 6) also did not improve the yield of toluene. Entries 8 and 9 demonstrate the effect of decreasing the amount of sodium iodide from 2 equiv. Decreasing NaI to 1 equiv



Figure 1. Copper-catalyzed hydrodehalogenation of 4-chlorotoluene. Performed using 20 mol % CuI, 1.5 equiv of ligand 1, 2 equiv of NaI, and acetonitrile as solvent at 200 °C using microwave radiation.

had little effect on the conversion of 4-chlorotoluene but reduced the yield of toluene to 55%, and some of the substrate was converted to products not observed by GC. When no NaI was present (entry 9), only 35% of the aryl chloride was consumed and the yield of toluene was reduced to 21%, corresponding to the amount of iodide present as CuI in the reaction. The 4-fold increase in the production of toluene between entry 1 and entry 9 is compelling evidence that the CTC method proposed in Scheme 3 is in operation and that the majority of the hydrodehalogenation takes place with 4-iodotoluene as the intermediate. When all isources of iodide are removed from the reaction by replacing CuI with CuCN (entry 10), the yield of toluene is 3% and only 12% of 4-chlorotoluene is consumed; 9% of the starting material is converted to 4-tolunitrile.

Additional evidence for the CTC hydrohalogenation mechanism was obtained by monitoring the amounts of 4-chlorotoluene, 4-iodotoluene, and toluene produced during the 2 h reaction time (Figure 1). In the first 20 min, the amount of 4-iodotoluene reaches a maximum at ~40 mol %, indicating that the rate of halogen exchange is faster than the rate of hydrodehalogenation. A similar reaction profile was seem by Buchwald in his work on the copper-catalyzed domino halogen exchange—cyanation of aryl bromides.⁶⁵

The optimized reaction conditions for hydrodehalogenation found in Table 3, entry 1, were applied to a variety of aryl bromides (Table 4) and aryl chlorides (Table 5). Substrates were chosen with consideration toward the ability of the corresponding arenes to be isolable by column chromatography when possible. Due to their high degree of structural similarity, complete separation of arenes from small amounts of aryl bromide and aryl chloride starting materials and aryl iodide catalytic intermediates was not possible; consequently, the reported isolated yields were adjusted for the presence of aryl halides. For aryl bromides (Table 4), consumption of 99% of substrate occurred after 1-2 h under hydrodehalogenation conditions. The methodology provided arenes in 35–84% yield. Encouragingly, both 4,4'-dibromobiphenyl and 4-bromobiphenyl, members of the PBB family, were hydrodehalogenated to give biphenyl in similarly high yields, 72% and 77%, respectively, if the 20 mol % CuI and 2 equiv of NaI per bromide atom in the substrate were maintained.

As with aryl bromides, aryl chloride substrates (Table 5) were nearly completely consumed under hydrodehalogenation

 Table 4. Microwave-Assisted Copper-Catalyzed Hydrodeha

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 Iodides





^{*a*} Determined by GC. ^{*b*} GC yield; average of two runs versus standard (*n*-decane or *n*-hexadecane). ^{*c*} No starting material detected by GC. ^{*d*} Average of two runs after isolation by column chromatography; isolated as a mixture of the arene and the aryl iodide; yield reported is corrected for the presence of aryl iodide. ^{*c*} Reaction conducted using 40 mol % CuI, 4 equiv of NaI, 3 equiv of ligand. ^{*f*} Reaction conducted using 10 mol % CuI.

conditions (89–99%) except for 2-chlorotoluene (entry 2, 54% conversion), where the steric hindrance of the methyl group prevented efficient conversion to 2-iodotoluene. However, it should be noted that 54% conversion of the 2-chlorotoluene starting material to toluene is \sim 5-fold greater than the conversion of 2-chlorotoluene to 2-iodotoluene in the absence of the hydrodehalogenation step (Table 2, entry 5), evidence that the CTC cycle is capable of shifting the equilibrium-limited halogen exchange toward aryl iodide. In general, aryl chlorides produced arenes in lower yields (12–80%) than their corresponding aryl bromides under the same reaction conditions.

The presence of functional groups containing oxygen or nitrogen heteroatoms (Table 4, entries 6-8, Table 5, entries 5-7) had a deleterious effect on the formation of arenes for both aryl bromide and aryl chloride substrates. In many cases, starting materials were converted to side products that were not observable and/or identifiable by GC-MS. Yields of arenes for these substrates could be improved by decreasing reaction time from 2

Table 5. Microwave-Assisted Copper-Catalyzed Hydrodeha-logenation of Aryl Chlorides via the in situ Formation of ArylIodides



^{*a*} Determined by GC. ^{*b*} GC yield; average of two runs versus standard (*n*-decane or *n*-hexadecane). ^{*c*} No starting material detected by GC. ^{*d*} Average of two runs after isolation by column chromatography; isolated as a mixture of the arene and the aryl iodide; yield reported is corrected for the presence of aryl iodide. ^{*c*} Reaction conducted using 40 mol % CuI, 4 equiv of NaI, 3 equiv of ligand. ^{*f*} Reaction conducted using 10 mol % CuI. ^{*g*} Reaction conducted using 20 mol % CuI, 4 equiv of NaI, 3 equiv of ligand.

to 1 h. For some substrates, the low yields were due in part to side reactions with products observable by GC. When 4-chlorobenzophenone and 4,4'-dichlorobenzophenone (Table 5, entries 3 and 4) were subjected to the CTC hydrodehalogenation conditions, a significant amount of an unidentifiable side product with a molecular ion peak of m/z = 194 was observed; this product was absent from reaction mixtures where 4-bromobenzophenone was the substrate, and subsequent experiments proved that this product was not formed from benzophenone itself under the reaction conditions. Both 5-bromoindole (Table 4, entry 7) and 5-chloroindole (Table 5, entry 6) crude product mixtures contained a compound identified by MS as indole dimer. In the case of 4-bromoanisole (entry 8) and 4-chloroanisole (entry 14), a portion of the starting material and the corresponding arene were subject to demethylation to give 4-halophenol and phenol. Evidence that the demethylation involved diamine ligand 1 was provided by GC-MS, where both N,N,N'-trimethylcyclohexane-1,2-diamine and N,N,N',N'-tetramethylcyclohexane-1,2-diamine were observed in the product mixture derived from 4-bromoanisole.

As seen from the conditions screened in Table 3, the yield of toluene formed in hydrodehalogenation of 4-chlorotoluene increased when the amount of diamine 1 was increased from 0.4 equiv to 1.5 equiv (entries 1 and 4). This observation suggested that 1 could be the hydrogen source for the hydrodehalogenation reaction. Previous literature reports of hydrodechlorination involving Cu(I)-*n*-butylamine catalyst system implicate the amine as the hydrogen source.⁷⁰ We attempted to determine the identity of the hydrogen source in our CTC hydrodehalogenation by conducting the reaction with 4-chloropropiophenone using 10 mol % CuI, 1.5 equiv of diamine 1, and 2 equiv of NaI in CD₃CN for 2 h at 200 °C. By MS, 70% of the propiophenone formed contained hydrogen, while the remaining 30% contained deuterium, supporting the hypothesis that ligand 1 is the major source of hydrogen for the reaction. The observation that some of the hydrogen source is derived from the solvent is not unprecedented. In the Cu(I)-mediated etherification of sterically hindered aryl iodides, Hartwig reported hydrodeiodinated products in which some portion of the hydrogen came from the solvent, DMSO*d*₆.⁷¹ The exact mechanism by which deuterium is incorporated in the CTC hydrodehalogenation remains to be explored, but H/D exchange between diamine 1 and solvent appears to be absent since neither mono- nor dideuterated 1 was observed by GC-MS as components of the unreacted ligand when the hydrodehalogenation of 4-chloropropiophenone was performed for only 10 min at 200 °C in CD₃CN. Analysis of the propiophenone formed after this short reaction time revealed that 20% contained deuterium; when the experiment was repeated with a reaction time of 5 min, only 9% of the arene formed was deuterated. These results suggest that 1 is the kinetically preferred hydrogen source. Another observation of interest is that this reaction mixture contained N,N,N'-trimethylcyclohexane-1,2-diamine, an indication that methylation of ligand 1 is occurring even in the absence of a substrate such as 4-bromoanisole. Future mechanistic studies will attempt to identify the source of the methyl group being transferred; the most likely possibilities are ligand 1 itself or the substrate, 4-chloropropiophenone.

In conclusion, we have described here a microwave-assisted CTC methodology for the hydrodehalogenation of aryl bromides and aryl chlorides where the first step of the tandem catalytic cycle is halogen exchange to form aryl iodides. Improvements to this methodology would include increasing the functional group tolerance of the reaction and identifying a less expensive ligand/hydrogen source than diamine 1, goals that could be furthered by conducting mechanistic studies of the hydrodehalogenation step. We also intend to extend the CTC methodology to other transformations by varying the second step of the tandem catalytic cycle to include carbon-carbon and carbon-nitrogen bond forming reactions. The formation of a small amount of 4-tolunitrile when CuCN was used as the catalyst (Table 3, entry 10) is promising since previous reports of cyanation of aryl chlorides using copper catalysts have been successful only with highly activated substrates.⁶⁶⁻⁶⁸ These results will be communicated in due course.

EXPERIMENTAL SECTION

General Considerations. All manipulations were carried out using standard nitrogen drybox techniques. Anhydrous acetonitrile, copper(I) iodide, and acetonitrile- d_3 were purchased from Acros and used as received. *trans-N,N'*-Dimethylcyclohexane-1,2-diamine was purchased from Aldrich and used as received. Microwave reactions were performed in a CEM Discover microwave reactor. GC-MS analysis was performed on a Shimadzu GCMS-QP5050A with a Restek Rxi-5 ms capillary column (30 m, 0.25 mm i.d., 0.25 μ m film thickness, 5% diphenyl/95% dimethylpolysiloxane) or Varian Saturn 2900 GC/3100 GC/MS/MS with a Varian VF-5 ms Factor Four capillary column (30 m, 0.25 mm i.d., 0.25 μ m film thickness, 5% diphenyl/95% dimethylpolysiloxane). ¹H and ¹³C NMR spectra were recorded on a JEOL ECX-400 spectrometer and were referenced to residual protio solvent peaks. Melting points were measured on an Electrothermal Meltemp melting point device.

General Procedure for the Copper-Catalyzed Conversion of Aryl Bromides into Aryl lodides. In a nitrogen-filled glovebox, CuI (15 mg, 0.079 mmol, 5 mol %), NaI (450 mg, 3.00 mmol), and an aryl bromide (1.5 mmol) were weighed into an oven-dried microwave tube containing a small stir bar. Acetonitrile (0.6 mL) was added by syringe. Then trans-N,N'-dimethylcyclohexane-1,2-diamine (23.7 µL, 0.1 mmol, 10 mol %) was added by positive displacement pipet, the sample was stirred, and a septum-lined cap was added. The initial reaction mixture appeared as a yellow or yellow-green liquid over a white solid. After removing the tube from the box, the reaction was performed in a CEM Discover microwave reactor for 30-120 min at 100 °C and 250 W (with power adjustments to maintain temperature), with a 2 min ramp time. After cooling, the reaction mixture contained a turquoise-blue liquid over a solid. After cooling, the product mixture was purified by column chromatography on silica. The yields reported did not take into account the trace amount of aryl bromide present in the isolated products.

General Procedure for the Copper-Catalyzed Conversion of Aryl Chlorides into Aryl lodides. In a nitrogen-filled glovebox, CuI (10 mg, 0.047 mmol, 5 mol %), NaI (300 mg, 2.00 mmol), and an aryl chloride (1.0 mmol) were weighed into an oven-dried microwave tube containing a small stir bar. Acetonitrile (0.5 mL) was added by syringe. Then trans-N,N'-dimethylcyclohexane-1,2-diamine (23.7 µL, 0.1 mmol, 10 mol %) was added by positive displacement pipet, the sample was stirred, and a septum-lined cap was added. The initial reaction mixture appeared as a yellow or greenish liquid over a white solid. After removing the tube from the box, the reaction was performed in a CEM Discover microwave reactor for 60 min at 200 °C and 250 W (with power adjustments to maintain temperature), with a 2 min ramp time. After cooling, the crude reaction mixture appeared as a yellow or brown solution. An equimolar amount (versus ArCl) of either hexadecane or decane was added to the solution. The solution was then quenched with 2 mL of water and 2 mL of EtOAc. The resulting solution was a dark brown, cloudy organic layer over a purple aqueous layer. A drop was removed from the organic layer and diluted with 10 drops of EtOAc in order to determine the GC yield.

General Procedure for the Copper-Catalyzed Conversion of Aryl Bromides and Aryl Chlorides into Arenes. In a nitrogenfilled glovebox, CuI (40 mg, 0.21 mmol, 20 mol %), NaI (300 mg, 2.00 mmol, 2 equiv), and an aryl bromide or aryl chloride (1.0 mmol) were weighed into an oven-dried microwave tube containing a small stir bar. Acetonitrile (0.5 mL) was added by syringe. Then trans-N,N'-dimethylcyclohexane-1,2-diamine (237 μ L, 1.5 mmol, 1.5 equiv) was added by positive displacement pipet, the sample was stirred, and a septum-lined cap was added. The initial reaction mixture appeared as a yellow or greenish liquid over a white solid. After removing the tube from the drybox, the reaction was performed in a CEM Discover microwave reactor for 1-2 h at 200 °C and 250-300 W (with power adjustments to maintain temperature), with a 5-10 min ramp time. Most reactions reached 200 $^{\circ}\mathrm{C}$ after ${\sim}2$ min. After the desired reaction time was reached and the tube cooled, the crude reaction mixture appeared as a dark brown liquid over some solids. The product mixture was either spiked with \sim 1.0 mmol of decane for GC yield determination or purified by column chromatography on silica gel. Products purified by column chromatography routinely contained a small percentage of the corresponding aryl iodide, measurable by GC and/or NMR and reported yields were adjusted to account for this impurity.

ASSOCIATED CONTENT

Supporting Information. Characterization data for all isolated products and experimental details for deuterium-labeling

experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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