Straightforward Solvent-Free Heterogeneous Palladium-Catalyzed Synthesis of Arylamines from Nonaromatic Substrates by Dehydrogenative Alkylation

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S *Supporting Information*

ABSTRACT: Arylamines can be synthesized in good to excellent yields, with selectivity from nonaromatic and easy available substrates as amines and cyclohexanone derivatives. The dehydrogenative alkylation was catalyzed by a heterogeneous and recyclable Pd/C catalyst, without additional solvent. No atmosphere of molecular oxygen was necessary, making the process safer than reported conditions under oxygen. Thus, the reactions were realized in nonaerobic conditions without any additive when starting from α-tetralones. For functionalized cyclohexanones, the addition of an alkene as a hydrogen scavenger was necessary, and the reaction could also be carried out under air. Besides, arylamines were also synthesized from nitro compounds by cross-dehydrogenative arylation under argon atmosphere. From experimental data, the key intermediate in these transformations seems to be an imine that is dehydrogenated to afford the final aromatic product.

KEYWORDS: Dehydrogenation, Alkylation, Heterogeneous catalysis, Palladium, Arylamines
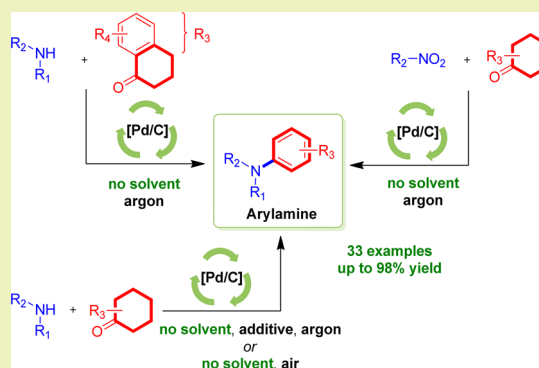
■ INTRODUCTION

Arylamines are an important class of compounds that find applications in various domains including pharmaceuticals, agrochemicals, dyes, or the electronic industry.[1−3] The nucleophilic aromatic substitution via a Meisenheimer[4,5] intermediate is one pathway to prepare this family of products. However, these noncatalyzed transformations are restricted to electron deficient aromatic rings even if an activation method is employed.[6,7] The addition of a metal in the reaction conditions contributed to overcome this limitation and thus enlarged the reaction scope. Since the pioneers works of Ullmann[8] and Goldberg,[9] improvements were realized in order to use catalytic quantities of copper.[10−12] However, despite the advantages linked to the price and low toxicity of copper, the employed conditions are often harsh. Alternatively, this metal is also widely used in the Chan−Lam-type conditions[13−15] for the coupling of tetrafluoroborate salts or silanes with amines. Palladium was later studied for the C−N bond formation. In 1983, Migita[16] described the palladium-catalyzed amination of aryl bromides. The next year, Boger[17] reported the synthesis of lavendamycin including an arylation step in the presence of a stoichiometric amount of palladium complex. Since 1995 and the development of the highly efficient Buchwald−Hartwig coupling reaction,[18,19] many studies were reported using this metal for amination reactions, and guidelines were recently proposed to establish the different parameters.[20−22] These reports offer a wide range of tools, and some of them have been industrially adapted.[23] Progress has also been made on the direct amination of the C−H bond.[24−26] However, the presence of stoichiometric quantities of bases implied a large production of wastes.

Concerning alternatives to these coupling methodologies, the aromatization of amine derivatives was also explored. In 1989, 2,6-dimethylaniline was synthesized from 2,6-dimethylcyclohexanone in gas phase in the presence of a palladium catalyst.[27] Ten years later, tetralones imines were aromatized in the presence of Pd/C.[28,29] This metal in stoichiometric quantity allows also the formation of aromatic amines from enamines.[30] A catalytic process was then proposed by Cossy[31] and Beller.[32] With the development of a more sustainable chemistry, the direct access in one step to aromatic derivatives from nonaromatic compounds has recently encountered great interest. Probably inspired by pioneers works,[33−40] Stahl has reported the aerobic dehydrogenation of cyclohexanone to phenol and the formation of meta-substituted phenols via a one-pot Heck/dehydrogenation reaction.[41−43] A tandem

reaction γ–C–H arylation–aromatization was also reported by Imahori.[44] In a continuous work concerning the aerobic aromatization of cyclohexenones,[45] the formation of aryl amines in one pot from ketones was studied. Yoshikai described the homogeneous palladium-catalyzed formation of aryl amines from cyclohexanones and amines under a molecular atmosphere of oxygen.[46] However, the yields were often moderate, and moreover, limitations were observed with substrates such as tetralones and 2-substituted cyclohexanones. Deng and Li reported the same year the formation of aryl amines from cyclohexanones or cyclohexenones with amines,[47] hydrazines,[48] or nitro[49] as partners. Except for reactions performed with nitro groups, all these efficient methodologies were realized under a molecular oxygen atmosphere implying flammability risks. Besides, homogeneous catalysts, solvents, and additives were also required in these examples, making them less interesting from both economical and environmental point of views. Finally, nonmetal catalyzed routes[50,51] were also reported notably by Maycock.[52,53]

In our continuous efforts to valorize cheap or biosourced raw materials as well as to develop eco-efficient processes for alkylation reactions,[54,55] we recently described the solvent-free dehydrogenative alkylation of cyclohexanones to prepare aryl ethers in the presence of a heterogeneous palladium catalyst.[56,57] During this study, one example concerning the formation of aryl amines was also reported (Scheme 1a).

Scheme 1. (a) Initial Observation Made during Our Preliminary Study and (b) Strategies Developed in This Work for the Preparation of Arylamines
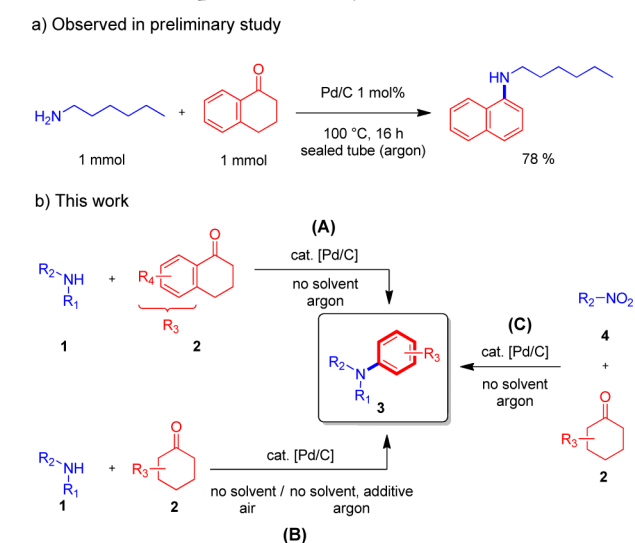
Consequently, it was interesting to optimize the reaction conditions with amines and then to explore the scope and limitations in order to propose a heterogeneous catalyzed alternative to the literature data. Notably, our aim was to avoid the utilization of an atmosphere of molecular oxygen in order to develop a safer process in which the catalyst can be easily removed and recycled. The optimization was realized on α-tetralone (A) and then extended to other tetralones and cyclohexanones (B). Finally, the possibility to start from nitro derivatives (C) was also studied (Scheme 1b).

EXPERIMENTAL SECTION

General Information. Amines, nitro compounds, cyclohexanone, and tetralone derivatives were purchased from Acros, Sigma-Aldrich, Alfa Aesar, and TCI. All reagents were used as received from the chemical company without further purification, excepted for aniline and nitrobenzene, which were distilled prior to use. Pd/C (5%) on activated carbon, reduced and dry (Escat 1431), and all the supported catalysts were purchased from Strem Chemicals and Sigma-Aldrich. The GC-MS analyses were performed on a Focus GC equipped with a DB-5MS capillary column (30 m, 0.25 mm i.d, 0.25 μm film thickness) and a DSQ mass spectrometer as detector. The carrier gas was helium, at a flow rate of 1 mL/min. Column temperature was initially 70 °C for 2 min, then gradually increased to 310 °C at 15 °C/min, and was finally kept at 310 °C for 10 min (injector temperature 220 °C and transfer line temperature 280 °C). For GC-MS detection, an electron ionization system was used, and the mass analyzer was a simple quadrupole.

General Procedures. *Dehydrogenative Alkylation of α-Tetralone with Amines (A).* In a sealed tube under argon, 3 mmol of α-tetralone derivative was added to 6 mmol of amine. Next, 64 mg of Pd/C (5%) (0.03 mmol, 1 mol %) was added to the mixture under an inert argon atmosphere. The medium was stirred at 130 °C for 16–36 h at 800 rpm, depending on the substrate. Thereafter, the crude was dissolved in a mixture of CH_2Cl_2 and CH_3OH and filtered off (Millipore Durapore filter 0.01 μm). The solvents were evaporated under reduced pressure, and the crude product was finally purified by flash chromatography on silica gel to afford the desired naphthylamine (eluent:cyclohexane/ethyl acetate = 100:0–9:1).

Dehydrogenative Alkylation of Functionalized Cyclohexanones and β-Tetralones in Nonaerobic Conditions (B). The same procedure as (A) was followed, but two molar equivalents of 1-octene were added under an inert argon atmosphere. The medium was stirred at 800 rpm at 130 °C for 16–36 h, depending on the substrate.
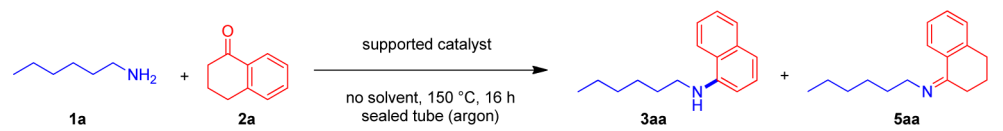
Dehydrogenative Alkylation of Functionalized Cyclohexanones and β-Tetralones in Aerobic Conditions (B). The same procedure as (A) was followed, but the reaction was carried out in a round-bottomed flask equipped with a condenser fitted with a $CaCl_2$ guard. The medium was stirred at 800 rpm at 130 °C for 16–48 h, depending on the substrate.

Cross-Dehydrogenative Alkylation of Functionalized Cyclohexanones with Nitro Compounds (C). In a sealed tube under argon, 30 mmol of cyclohexanone derivative was added to 3 mmol of nitro compound. Next, 160 mg of Pd/C (5%) (0.075 mmol, 2.5 mol %) was added to the mixture under an inert argon atmosphere. The medium was stirred at 150 °C for 16–36 h at 800 rpm, depending on the substrate. Thereafter, the crude was dissolved in a mixture of CH_2Cl_2 and CH_3OH and filtered off (Millipore Durapore filter 0.01 μm). The solvents were evaporated under reduced pressure, and the crude product was finally purified by flash chromatography on silica gel to afford the desired arylamine (eluent:cyclohexane/ethyl acetate =100:0–9:1).

Full experimental details and spectral data for all compounds are provided in the Supporting Information.

RESULTS AND DISCUSSION

As a model study, the solvent-free dehydrogenative arylation of hexylamine **1a** with α-tetralone **2a** was performed in a molar ratio of 5:1 at 150 °C in nonaerobic conditions under an argon atmosphere. The first consideration was the influence of the heterogeneous metal catalyst on the arylamine formation (Table 1). With rhodium catalysts, the main product observed was imine **5aa**, and whatever the support, only traces of the expected naphthylamine **3aa** were measured (entries 1 and 2). Similar results were obtained with supported ruthenium catalysts (entries 3 and 4), and no traces of **3aa** were measured with Ir/C (entry 5). Better results were observed with palladium catalysts (entries 6 and 7), and finally, the desired naphthylamine **3aa** was obtained in 86% yield after 16 h with 1

Table 1. Influence of Catalyst and Temperature for Dehydrogenative Alkylation of α-Tetralone 2a with Hexylamine 1a[a]

					yield (%)[b]	
entry	catalyst	amount (mol %)	temp (°C)	conversion (2a, %)[b]	3aa	5aa
1	Rh/Al$_2$O$_3$ (5%)	1	150	78	2	76
2	Rh/C (5%)	1	150	62	2	60
3	Ru/Al$_2$O$_3$ (5%)	1	150	62	0	62
4	Ru/C (5%)	1	150	60	0	60
5	Ir/C (1%)	1	150	34	0	34
6	Pd/SiO$_2$ (5%)	1	150	73	3	70
7	Pd/Al$_2$O$_3$ (5%)	1	150	78	10	68
8	Pd/C (5%)	1	150	>99	86	0
9	Pd/C (5%)	1	130	>99	90	0
10	Pd/C (5%)	1	100	>99	89	0
11	Pd/C (5%)	1	80	>99	36	64
12	Pd/C (5%)	1	60	>99	3	97
13	Pd/C (5%)	2	130	>99	75	0
14	Pd/C (5%)	0.5	130	95	10	85
15	carbon[c]	–	130	81	0	81
16	–	–	130	96	0	96
17	–	–	60	51	0	51

[a]Conditions: molar ratio α-tetralone 2a/hexylamine 1a 1:5, catalyst, 16 h, sealed tube (argon). [b]Conversions and yields were determined by ^{1}H NMR spectroscopy. [c]Purity ≥99.5%; added in 20 wt %.

mol % of palladium on charcoal (entry 8). This is in agreement with the previous conditions developed in the laboratory for the preparation of arylethers.[56,57] To determine the best experimental parameters, reaction of 1a was carried out with 2a at different temperatures and Pd/C loadings. Thus, at 130 and 100 °C, the yields for the desired arylamine 3aa were slightly improved to 90%, indeed less dehydration and dehydrogenation byproducts of the starting α-tetralone 2a as 1,2,3,4-tetrahydronaphthalene, naphthol, and naphthalene were formed in these cases (entries 9 and 10). At lower temperatures, the reaction rate was lower, and imine 5aa was observed as the major product (entries 11 and 12). With 2 mol % of Pd/C, the selectivity for the desired arylamine decreased because higher quantities of degradation products of α-tetralone 2a were observed. Thus, the desired naphthylamine 3aa was observed in a lower yield of 75% (entry 13). With 0.5 mol % of Pd/C, the dehydrogenation rate decreased, and imine 5aa was obtained in 85% yield (entry 14). To have an insight into the specific role of the Pd/C catalyst, a reaction with a classic activated carbon as catalyst gave only compound 5aa in 81% yield (entry 15), whereas a catalyst-free attempt afforded imine 5aa in 96% yield (entry 16). By carrying out reactions at lower temperature (60 °C), the Pd/C had a positive effect on the imine formation because only 51% of imine 5aa were obtained without catalyst (entry 17), whereas 97% of 5aa were observed with 1 mol % of Pd/C in the same conditions (entry 12).

As the reaction was carried out under solvent-free conditions, the amount of amine 1a was also considered. Best results were obtained with molar ratios α-tetralone 2a/hexylamine 1a above 1:2. With a stoichiometric amount of reagents, the yield for 3aa decreased to 81%. Thus, the best conditions were defined by mixing one equivalent of α-tetralone derivative 2 with two equivalents of amine 1 in the presence of 1 mol % of Pd/C at

130 °C for 16 h in a closed system under nonaerobic conditions. In an open reactor under air, the reaction time was longer (48 h) to reach 80% conversion to naphthylamine 3aa. This lower reaction rate was probably linked to a partial oxidation of the Pd/C catalyst under air.

As can be seen on the GC/MS spectrum of the crude after complete conversion in optimized conditions (Figure 1), the dehydrogenative alkylation of α-tetralone 2a with hexylamine 1a gave product 3aa with a good selectivity of 92%. 1,2,3,4-Tetrahydronaphthalene 6 was observed as byproduct of the reaction as well as traces of trihexylamine 7. Byproduct 6 came
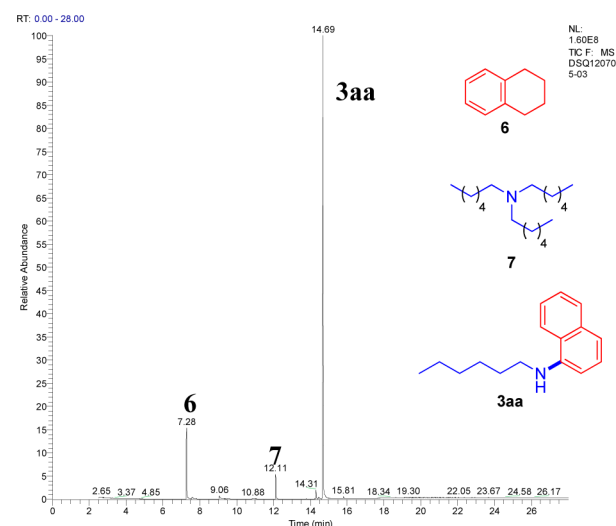

Figure 1. GC/MS chromatogram of the reaction medium from the dehydrogenative alkylation of α-tetralone 2a with hexylamine 1a in optimized conditions.

certainly from the dehydration of α-tetralone followed by the hydrogenation of the double bond. As an excess of hexylamine **1a** was used in the reaction, a small amount of hexylamine can be dehydrogenated under these conditions into the corresponding imine, allowing the addition of a second and a third hexylamine in order to afford the tertiary amine with release of ammonia.

With the best conditions in hands, the scope of this transformation was evaluated with various amines (Table 2).

Table 2. Scope of Dehydrogenative Alkylation of α-Tetralones 2 with Amines[a]

Entry	Amine		Product		Yield (%)[b]
1		**1a**		**3aa**	86 (90)
2		**1b**		**3ba**	91 (98)
3		**1c**		**3ca**	59 (62)
4		**1d**		**3da**	58 (60)
5[c]		**1e**		**3ea**	58 (70)
6		**1f**		**3fa**	22 (31)
7		**1g**		**3ga**	67 (71)
8		**1a**		**3ab**	73 (80)
9		**1a**		**3ac**	86 (88)

[a]Conditions: molar ratio α-tetralone **2**/amine **1** 1:2, Pd/C (5%) 1 mol %, 130 °C, 16 h, sealed tube (argon). [b]Isolated yield; ^{1}H NMR yield in parentheses. [c]molar ratio **2a**/**1e** = 2.5:1, Pd/C (5%) 2 mol %.

Aliphatic primary amines were arylated in good isolated yields, as hexylamine **1a** and cyclohexylamine **1b** (entries 1 and 2). With benzylamine **1c**, product **3ca** was isolated in 59% (entry 3). This lower yield was explained by the formation of 1-aminonaphthalene in 30% yield by in situ debenzylation mediated by the palladium catalyst, as already reported by Janin and co-workers.[58] The reaction with aniline **1d**, which is less nucleophile, afforded the corresponding amine **3da** in 58%

isolated yield (entry 4). Hexamethylenediamine **1e** was a suitable substrate when performing the reaction in a molar ratio **2a**/**1e** of 2.5:1 with 2 mol % of Pd/C, giving **3ea** in 58% yield (entry 5). Secondary cyclic amines were also tested. The dehydrogenation alkylation with piperidine **1f** gave product **3fa** in only 22% isolated yield, with a moderate conversion of α-tetralone **2a** and the formation of complex byproducts (entry 6).

Surprisingly, the reaction with N,N-dibutylamine **1g** afforded compound **3ga** in 67% yield (entry 7). The steric hindrance of the substrates as well as the possibility to dehydrogenate the starting amine (Figure 1) can explain the loss of a butyl chain in the reaction between N,N-dibutylamine **1g** and α-tetralone **2a** (Table 2, entry 7), as proposed in Scheme 2. The direct

Scheme 2. Proposed Mechanism for the Reaction of α-Tetralone 2a with N,N-Dibutylamine 1g
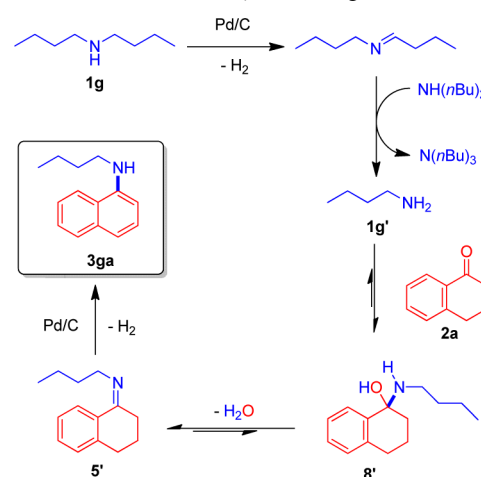
dehydrogenation of the secondary amine **1g** to the secondary imine can afford butylamine **1g′** by SN$_2$ reaction. Thus, the less hindered primary butylamine reacts with α-tetralone **2a**, giving imine **5′**, which undergoes a dehydrogenation reaction to afford naphthylamine **3ga** in good yield. This proposition was confirmed by the reaction of N,N-dibutylamine with naphthalene as an inert partner under the same conditions that gave a mixture of tributylamine and butylamine.

Finally, α-tetralone derivatives could also be successfully converted to the corresponding arylamines with hexylamine **1a**. The presence of a methoxy or a methyl group on the α-tetralone did not affect the efficiency of the reaction, and products **3ab** and **3ac** were isolated in good 73% and 86% yields, respectively (entries 8 and 9).

In order to increase the scope of the reaction, the amination of cyclohexanone **2d** was explored (Table 3). Unfortunately, a lower yield of 67% was obtained for aryl amine **3ad** from hexylamine **1a** in nonaerobic conditions at 150 °C (entry 1). Besides, decomposition byproducts were also observed. By decreasing the temperature, the selectivity for **3ad** dropped dramatically, and the hydrogenated secondary amine **8ad** was obtained as the major product (entries 2 and 3). Consequently, by adding 1-octene in the reaction medium as a hydrogen scavenger, the expected arylamine could be detected in up to 91% yield when two molar equivalents were introduced (entry 4). The dehydrogenative alkylation was also efficient with styrene or methyl oleate as additives. The same selectivity for the desired arylamine **3ad** was observed, but the reaction rates

Table 3. Optimization of Conditions for Cyclohexanone 2d and β-Tetralone 2e[a]

Entry	Reactor type	Substrate	T (°C)	Additive	Conv. (2, %)[b]	Ratio (%)[b]		
						3	**5**	**8**
1	Sealed tube (argon)	2d	150	-	>99	67	0	10
2	Sealed tube (argon)	2d	130	-	>99	31	0	67
3	Sealed tube (argon)	2d	100	-	>99	33	0	67
4	Sealed tube (argon)	2d	130	1-octene (2 eq)	>99	91	0	7
5[c]	Open reactor (air)	2d	130	-	>99	75	0	14
6[d]	Open reactor (air)	2d	130	-	15	0	15	0
7	Sealed tube (argon)	2e	130	-	>99	30	0	70
8	Sealed tube (argon)	2e	130	1-octene (2 eq)	>99	98	0	0
9	Open reactor (air)	2e	130	-	>99	98	0	0

[a]Conditions: molar ratio cyclohexanone derivative **2**/hexylamine **1a** 1:2, Pd/C (1 mol %), 16 h. [b]Conversions and ratios were determined by ^{1}H NMR spectroscopy. [c]Reaction time = 60 h. [d]Reaction without Pd/C.

were lower, particularly for methyl oleate the complete conversion was reached after 48 h. It was also possible to replace the alkene by the molecular oxygen from air when carrying out the reaction in an open reactor. But in this case, the reaction time was longer, and complex byproducts were also formed. This could be linked to a partial oxidation of the Pd/C catalyst by the molecular oxygen from the air. Thus, product **3ad** was observed in 75% yield after 60 h (entry 5). When the Pd/C catalyst was removed under these last conditions, the conversion to the unwanted imine **5ad** was poor, and no arylamine **3ad** was detected (entry 6). Finally, the reaction with β-tetralone **2e** under nonaerobic conditions without additive afforded a mixture of aromatic and non-aromatic products (entry 7). This result suggests that the aromatization rate of β-tetralone is lower than in the case of α-tetralone, necessitating the addition of a hydrogen acceptor.

As expected, the best conditions found for β-tetralone **2e** were obtained when the reaction was performed in nonaerobic conditions with an alkene as additive (entry 8) or in aerobic conditions in an open reactor (entry 9). In both cases, the reaction was complete after 16 h with an excellent selectivity for the desired naphthylamine **3ae**.

Thus, two conditions (nonaerobic and aerobic) were retained for the dehydrogenative alkylation of cyclohexanone and β-tetralone derivatives, as summarized in scheme 3.

Subsequently, the scope of the dehydrogenative alkylation of cyclohexanone with various amines was investigated (Table 4). Primary amines such as hexylamine **1a** and cyclohexylamine **1b** afforded the arylamines products **3ad** and **3bd** in high yields in nonaerobic conditions (entries 1 and 2). Product **3ad** was also obtained in 69% yield in open reactor without additive (entry 1). When aniline was engaged, the corresponding diarylamine
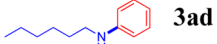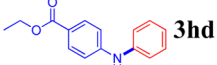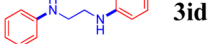
Scheme 3. Optimized Conditions for Preparation of Arylamines from Cyclohexanones: under Argon in Sealed Tube, with 1-Octene as Additive and under Air in Open Reactor
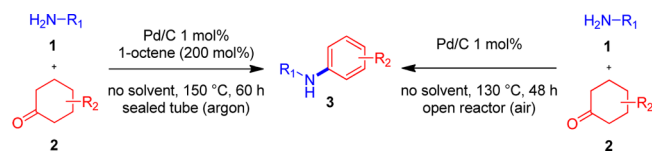
3dd was isolated in 52% yield, and the hydrogenated amine **8dd** was observed as byproduct (entry 3). The arylation rate was probably slower in this case. The reaction was efficient with a less nucleophilic aniline **1h** substituted in *para* position with an electron-withdrawing group, giving product **3hd** in 74% yield after a longer reaction time of 36 h (entry 4). The reaction with ethylenediamine **1i** was slow and less selective, giving the desired diarylated diamine **3id** in 28% yield (entry 5). A poor yield of 23% was also obtained for the reaction with piperidine **1f** (entry 6). Besides, around 20% of the unwanted hydrogenated amine was also detected. The arylation of N,N-dibutylamine **1g** afforded the expected tertiary amine **3gd** in 45% yield, whereas the secondary amine was detected in less than 20% yield (entry 7). When comparing this result with the reaction performed with α-tetralone (Table 2, entry 7), this could be explained by a lower steric hindrance of the cyclohexanone **2d**.

Limitations of this method were observed in the case of worse nucleophilic amines as imidazole, pyrrole, and indole: no desired products were detected.

Table 4. Scope of Dehydrogenative Alkylation of Cyclohexanone 2d with Various Amines[a]
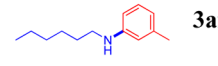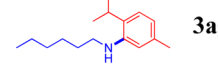
Pd/C (1 mol%)
1-octene (200 mol%)
no solvent, 130 °C, 16 h
sealed tube (argon)
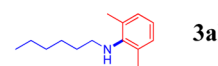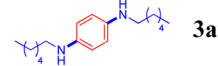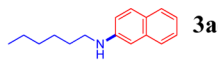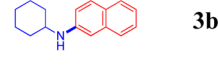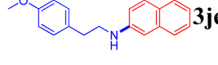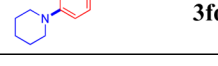
Entry	Amine		Product		Yield (%)[b]
1		1a		3ad	86 (91) 69[c] (75)
2		1b		3bd	98 (99)
3[d]		1d		3dd	52 (57)
4[d]		1h		3hd	74 (78)
5[e]		1i		3id	28 (32)
6[d]		1f		3fd	23 (26)
7[d]		1g		3gd	45 (50)

[a]Conditions: molar ratio cyclohexanone derivative 2/amine 1 1:2, 1-octene (200 mol %), Pd/C (5%) 1 mol %, 130 °C, 16 h, sealed tube (argon). [b]1H NMR yields in parentheses. [c]Reaction in open reactor (air) without additive. [d]Reaction time = 36 h. [e]molar ratio 1i/2d = 1:2.2, 1-octene (400 mol %), Pd/C (5%) 2 mol %.

Table 5. Scope of Dehydrogenative Alkylation of Cyclohexanone Derivatives with Amines[a]

Pd/C (1 mol%)
1-octene (200 mol%)
no solvent, 130 °C, 16 h
sealed tube (argon)

Entry	Cyclohexanone		Product		Yield (%)[b]
1		2f		3af	82 (87) 66[c] (71)
2[d]		2g		3ag	97 (99)
3[d]		2h		3ah	69 (79)
4[e]		2i		3ai	82 (87)
5		2e		3ae	97 (98) 95[c] (98)
6		2e		3be	81 (96)
7		2e		3je	70 (78)
8		2j		3fd	59 (67)

[a]Conditions: molar ratio cyclohexanone derivative 2/amine 1 1:2, 1-octene (200 mol %), Pd/C (5%) 1 mol %, 130 °C, 16 h, sealed tube (argon). [b]1H NMR yields in parentheses. [c]Reaction in open reactor (air) without additive. [d]Reaction time = 36 h. [e]Pd/C (5%) 2 mol %. [e]molar ratio 1/2 = 2.2:1; 1-octene (400 mol %), Pd/C (5%) 2 mol %.

As can be seen from the results in Table 5, hexylamine 1a was also arylated with substituted cyclohexanones. The reaction of 3-methylcyclohexanone 2f gave product 3af in 82% isolated yield under nonaerobic conditions and in 66% yield in open reactor (entry 1). Moreover, sterically hindered 2-substituted substrates as 2g and 2h were well alkylated after a longer reaction time of 36 h, yielding the desired arylamines 3ag and 3ah in 97% and 69%, respectively (entries 2 and 3). For 1,4-cyclohexanedione 2i, the dialkylated product 3ai was obtained in 82% yield when adding 2.2 mol equiv of hexylamine 1a (entry 4), and the reaction was also efficient with β-tetralone 2e and different primary amines 1a, 1b, and 1j (entries 5−7). As already observed,[47] the efficiency of the reaction with piperidine 1f could be improved when using 2-cyclohexen-1-one 2j as substrate, giving 3fd in 59% yield (entry 8). In this case, the dehydrogenation rate of the ring was probably higher than in the reaction with cyclohexanone 2d (Table 4, entry 6).

On the basis of the results as well as on the literature data,[31] a mechanism could be proposed for this transformation under aerobic and under nonaerobic conditions (Scheme 4). The first step in both pathways is the condensation of the amine and the cyclohexanone derivative to afford imine 5, and the Pd/C catalyst certainly increases the rate of this reaction (Table 1, entries 12 and 17, and Table 3, entry 6). Enamine 9 is then

generated through tautomerization of 5, and two consecutive dehydrogenation reactions catalyzed by the palladium surface afford the desired arylamine 3. An α-palladation of enamine 9 followed by a β-hydride-elimination is commonly proposed for this reaction in homogeneous catalysis.[46,47] In this case, the heterogeneous Pd(0) catalyst could adsorb on the surface the molecular hydrogen formed during the dehydrogenation/aromatization step. Depending on the operating conditions (i.e., nonaerobic or aerobic atmosphere), the adsorbed hydrogen is consumed by the alkene additive or by the molecular oxygen from the air. When no hydrogen acceptor was added in the medium in a sealed reactor, the released hydrogen can hydrogenate imine 5 or enamine 9 into the saturated secondary amine 8.

Contrary to what we observed in our previous works for the preparation of arylethers by dehydrogenative alkylation under aerobic conditions,[56,57] when carrying out the reaction of cyclohexanone 2d and hexylamine 1a under aerobic conditions, the reaction rate and the selectivity for the desired arylamine was lower (Table 3, entry 5). A conversion versus time curve showed that the hydrogenated amine 8ad was first formed as a major product before being probably partially converted to the desired arylamine 3ad thanks to the presence of O₂ as a hydrogen scavenger, thus explaining the longer reaction time required (Figure 2a). This observation was already reported for the preparation of anilines by dehydrogenation in a pioneer

1468

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Scheme 4. Proposed Mechanisms for Dehydrogenative Alkylation of a Cyclohexanone Derivative with an Amine Catalyzed by Pd/C in Open Reactor under Air (left) and in a Sealed Reactor under Argon without and with a Hydrogen Acceptor (right)
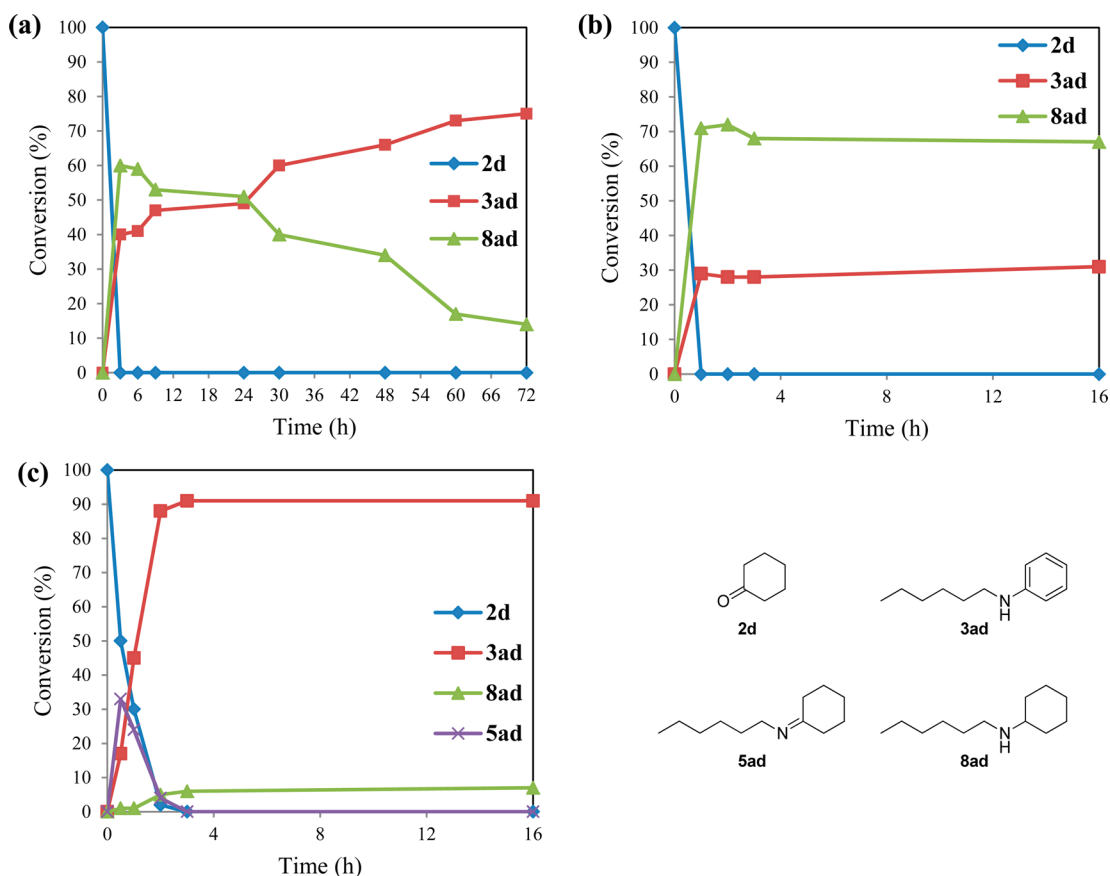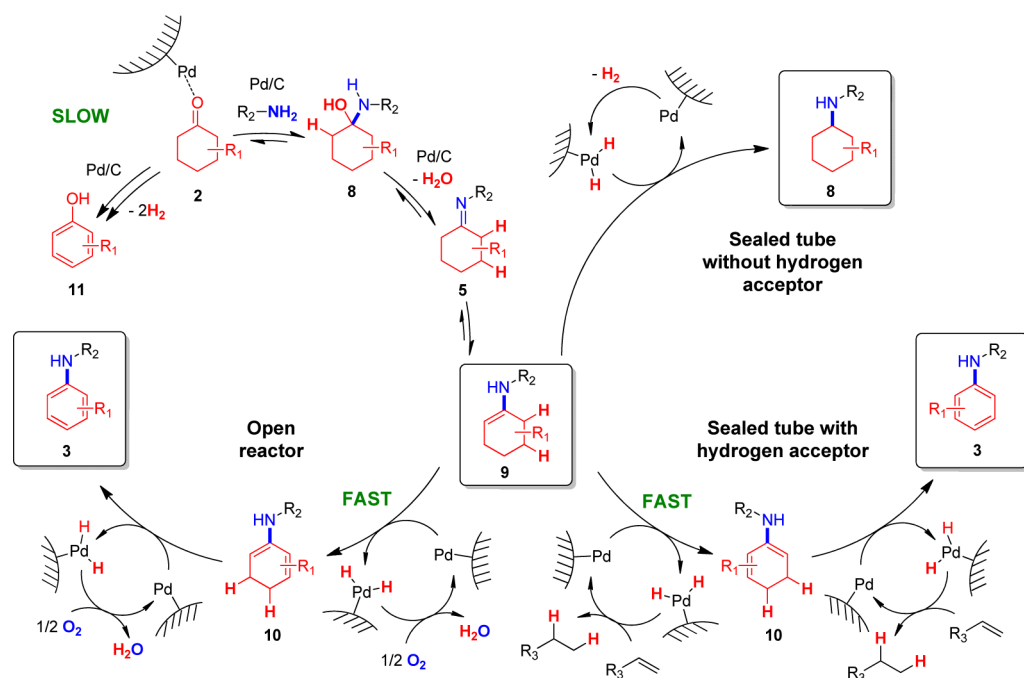
Figure 2. Reaction of cyclohexanone **2d** with hexylamine **1a** (a) in open reactor without additive (Table 3, entry 5), (b) in sealed tube under argon (Table 3, entry 2), and in sealed tube with 2 equiv of 1-octene (Table 3, entry 4) followed by ^{1}H NMR.

work.[27] The partial oxidation of the Pd/C catalyst by the molecular oxygen from the air may explain the decrease of the dehydrogenation rate of the cycle, allowing the partial

hydrogenation of imine **5** or enamine **9**. However, complex byproducts were also observed under these conditions. Control experiments using N-ethylcyclohexylamine as the sole substrate

1469

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of the reaction under both nonaerobic and aerobic conditions afforded the desired arylamine in only 10% yield and also a complex mixture of byproducts. Therefore, other intermediates probably play a key role in this transformation, like imine **5** or enamine species **9** and **10**. In fact, imine **5ad** could be aromatized under the optimized conditions. In a sealed reactor under argon without an additive (Figure 2b) or with 2 equiv of 1-octene (Figure 2c), the ratio hydrogenated amine **8ad**/arylamine **3ad** did not change throughout the reaction course. The more diluted medium in the last case decreased the reaction rate, and thus, intermediate imine **5ad** was observed at the beginning of the reaction.

Finally, it was interesting to test the borrowing hydrogen methodology from nitroarenes and cyclohexanones in these heterogeneous and solvent-free conditions, thus avoiding the utilization of toxic NMP as solvent and homogeneous catalysis conditions.[49] Indeed, the reduction of nitro to amine is possible with the hydrogen released by dehydrogenation of a small amount of the starting cyclohexanone, involving the condensation of both substrates to afford an intermediate imine. The desired arylamine is then obtained after tautomerization and dehydrogenation reactions on the palladium surface. Thus, no hydrogen scavenger is necessary in this case.

The investigation was realized with nitrobenzene **4d** and cyclohexanone **2d** without any solvent in a sealed tube under argon atmosphere at 150 °C (Table 6). At high molar ratio

Table 6. Optimization for Nitrobenzene 4d and Cyclohexanone 2d[a]
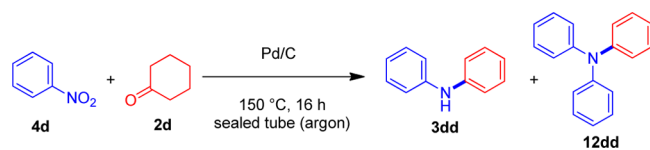
entry	Pd/C (mol %)	ratio **4d/2d**	conv. (**4d**, %)[b]	yield (%)[b] 3dd	yield (%)[b] 12dd
1	1	1/2	66	48	18
2	2	1/2	64	49	15
3	2.5	1/2	61	50	11
4	1	1/5	93	79	14
5	2.5	1/5	84	76	7
6	2.5	1/10	>99	99	1

[a]Conditions: Pd/C, 150 °C, 16 h, sealed tube (argon). [b]Conversions and yields were determined by ^{1}H NMR spectroscopy.

nitro/ketone of 1:2 and with 1 mol % of Pd/C, the conversion was 66% after 16 h. Diarylamine **3dd** was obtained as major product in 48% yield, but the unwanted triarylamine **12dd** was also detected in 18% yield, whereas only traces of phenol **11** (1−2%) were observed (entry 1). Thus, the reaction was certainly initiated by the dehydrogenation of a small amount of cyclohexanone into the phenol. By increasing the amount of catalyst to 2.5 mol %, the conversion decreased slightly, but a better selectivity for product **3dd** was observed (entries 2−3). The conversion could be improved with a lower molar ratio of **4d/2d** (entries 4−5), and finally, the best result was obtained when one molar equivalent of nitrobenzene **4d** was reacted with 10 mol equiv of cyclohexanone **2d** (entry 6). Under these conditions, the conversion was complete after 16 h, and the reaction afforded diarylamine **3dd** with an excellent selectivity. After complete conversion, traces of phenol **11** were also measured, and the unreacted cyclohexanone in excess was

recycled. Aliquots were also collected at low conversion to see if any intermediate could be characterized, but only products **3dd**, **12dd**, phenol **11**, as well as the unreacted reactants **4d** and **2d** were observed. Thus, the intermediate aniline **1d** was then certainly quickly converted into the diarylamine.

To further explore the scope of this cross-dehydrogenative alkylation, cyclohexanone derivatives were reacted with various nitro compounds in the optimized conditions (Table 7). The

Table 7. Scope of Solvent-Free Dehydrogenative Alkylation of Cyclohexanone Derivatives 2 with Nitro Compounds[a]

Entry	Nitro / cyclohexanone		Product		Yield (%)[b]
1		**4d**		**3dd**	98 (99)
2		**4k**		**3kd**	73 (79)
3		**4l**		**3ld**	94 (95)
4		**4m**		**3md**	58 (75)
5		**2f**		**3df**	95 (96)
6		**2k**		**3dk**	98 (99)
7[c]		**2a**		**3da**	91 (93)
8		**4n**		**3nd**	- (< 1)
9		**4o**		**3od**	- (20)

[a]Conditions: molar ratio nitro **4**/cyclohexanone derivative 1/10, Pd/C (5%) 2.5 mol %, 150 °C, 16 h, sealed tube (argon). [b]^{1}H NMR yields in parentheses. [c]Reaction time = 36 h.

reaction was efficient with *para*-substituted nitroarenes bearing electron-donating groups (**3kd**, entry 2) or electron-withdrawing groups (**3ld**, entry 3). However, when methyl 4-nitrobenzoate **4m** was used, the corresponding diarylamine **3md** was obtained in a lower yield of 58% (entry 4). Substituted cyclohexanone derivatives were also tested, and the reaction occurred regardless of the nature and position of the substituent (**3df**, **3dk**, entries 5 and 6). A longer reaction time was required when α-tetralone **2a** was used as starting material, probably because only one equivalent of molecular hydrogen was released in the medium by dehydrogenation reaction of the cycle (entry 7). Unfortunately, no conversion was observed with aliphatic nitro as nitrononane **4n** under these conditions (entry 8), whereas only 20% of the desired arylamine **3od** was detected with ethyl nitroacetate **4s** (entry 9). In this last example, the conversion was complete, but the reaction also afforded a complex mixture of byproducts.

From both environmental and economic point of views, these reactions were advantageously catalyzed by a heteroge-

neous Pd/C catalyst. Consequently, the recyclability of the catalyst was evaluated with model substrates hexylamine **1a** and α-tetralone **2a**. After each reaction, the crude was first diluted in a minimum of dichloromethane (CH$_2$Cl$_2$) and methanol (CH$_3$OH) and then filtered under argon flow. Next, the Pd/C catalyst was transferred in a new reactor under an argon flow for 2 h at room temperature. Once all solvents were evaporated, a new reaction was started with both substrates. CH$_2$Cl$_2$ and CH$_3$OH were chosen for the filtration because of their low boiling points and their ability to dissolve all the products, but the catalyst's filtration was also performed with biosourced ethanol. In this case, the Pd/C drying process under argon flow required a longer time of 4−6 h. After four reuses of the Pd/C catalyst, the yield for the desired naphthyl amine **3aa** slightly decreased to 76%. This slight decrease may be attributed to two factors. On one hand, the formation of complex decomposition byproducts in low amounts after each reaction was observed. These byproducts may precipitate and accumulate on the catalytic sites after each run. On the other hand, a low amount of palladium could be leached in the medium after each reuse. In fact, in our previous study reporting the preparation of arylethers by dehydrogenative alkylation,[56,57] an ICP-MS analysis of the crude showed that very low amounts of palladium were leached in the reaction mixture after each run (<10 ppm), without impacting the reaction yields. As amines are much better ligands than alcohols or ethers, it is possible that the Pd-leaching in this case can be higher.
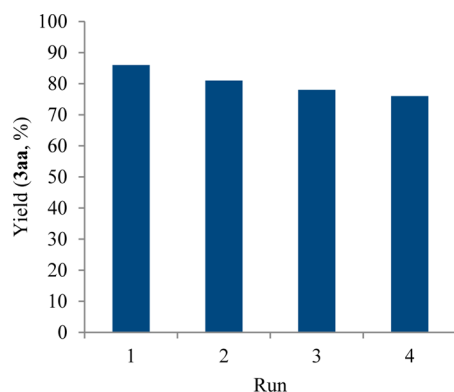

Figure 4. Catalyst recycling experiments.

CONCLUSION

In summary, we have developed three complementary solvent-free heterogeneous palladium-catalyzed procedures for the preparation of arylamines. The products were prepared by dehydrogenative alkylation of cyclohexanone derivatives with various amines or nitro compounds in safe conditions, without the need of an atmosphere of molecular oxygen linked to flammability risks. Thus, from α-tetralone derivatives, naphthyl-amines were synthesized under nonaerobic conditions without any additive, whereas the addition of an alkene was necessary as hydrogen scavenger when the reaction was carried out with substituted cyclohexanones and β-tetralones. It was also possible to perform the reaction in an open reactor under air and the Pd/C catalyst could be easily recycled several times. Finally, the same heterogeneous catalytic system was also highly efficient for an alternative solvent-free cross-dehydrogenative arylation of nitro compounds with cyclohexanones in a closed

system under argon atmosphere. On the basis of results obtained by additional experiments, a mechanism involving the formation of an imine that is dehydrogenated to the desired product could be proposed. Thus, these protocols could represent a convenient alternative to the existing cross-coupling reactions for the straightforward preparation of aryl- and diarylamines.

ASSOCIATED CONTENT

Ⓢ Supporting Information

Full experimental details and spectral data (^{1}H NMR, ^{13}C NMR, IR, HRMS) for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

REFERENCES

(1) Magano, J.; Dunetz, J. R. Large-scale applications of transition metal-catalyzed couplings for the synthesis of pharmaceuticals. *Chem. Rev.* **2011**, *111*, 2177−2250.

(2) Ricci, A. *Amino Group Chemistry: From Synthesis to the Life Sciences*; Wiley-VCH: Weinheim, 2008.

(3) Lawrence, S. A. *Amines: Synthesis Properties and Applications*; Cambridge University Press: Cambridge, 2004.

(4) Meisenheimer, J. Ueber reactionen aromatischer nitrokorper. *Justus Ann. Chem.* **1902**, *323*, 205.

(5) Bunnett, J. F.; Zhaler, R. E. Aromatic nucleophilic substitution reactions. *Chem. Rev.* **1951**, *49*, 273−412.

(6) Lanver, A.; Schmalz, H.-G. Microwave-assisted amination of a chloropurine derivative in the synthesis of acyclic nucleoside analogues. *Molecules* **2005**, *10*, 508−515.

(7) Singh, R.; Allam, B. K.; Raghuvanshi, D. S.; Singh, K. N. Cooperatively assisted *N*-arylation using organic ionic base−Brønsted acid combination under controlled microwave heating. *Tetrahedron* **2013**, *69*, 1038−1042.

(8) Ullmann, F. Ueber eine neue bildungsweise von diphenylamin-derivaten. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382−2384.

(9) Goldberg, I. Ueber phenylirungen bei Gegenwart von kupfer als katalysator. *Ber. Dtsch. Chem. Ges.* **1906**, *39*, 1691−1692.

(10) Beletskaya, I. P.; Cheprakov, A V. Copper in cross-coupling reactions the post-Ullmann chemistry. *Coord. Chem. Rev.* **2004**, *248*, 2337−2364.

(11) Monnier, F.; Taillefer, M. Catalytic CC, CN, and CO Ullmann-type coupling reactions: Copper makes a difference. *Angew. Chem., Int. Ed.* **2009**, *48*, 6954−6971.

(12) Evano, G.; Blanchard, N.; Toumi, M. Copper-mediated coupling reactions and their applications in natural products and designed biomolecules synthesis. *Chem. Rev.* **2008**, *108*, 3054−3131.

(13) Ley, S. V.; Thomas, A. W. Modern synthetic methods for copper-mediated C(aryl)-O, C(aryl)-N, and C(aryl)-S bond formation. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400−5449.

(14) Qiao, J. X.; Lam, P. Y. S. Copper-promoted carbon−heteroatom bond cross-coupling with boronic acids and derivatives. *Synthesis* **2011**, 829−856.

(15) Miki, Y.; Hirano, K.; Satoh, T.; Miura, M. Copper-catalyzed electrophilic amination of arylsilanes with hydroxylamines. *Org. Lett.* **2013**, *15*, 172−175.

(16) Kosugi, M.; Kameyama, M.; Migita, T. Palladium-catalyzed aromatic amination of aryl bromides with N,N-diethylaminotributyltin. *Chem. Lett.* **1983**, 927−928.

(17) Boger, D. L.; Panek, J. S. Palladium (0) mediated β-carboline synthesis: Preparation of the CDE ring system of Lavendamycin. *Tetrahedron Lett.* **1984**, *25*, 3175−3178.

(18) Louie, J.; Hartwig, J. F. Palladium-catalyzed synthesis of arylamines from aryl halides-mechanistic studies lead to coupling in the absence of tin reagents. *Tetrahedron Lett.* **1995**, *36*, 3609−3612.

(19) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. A simple catalytic method for the conversion of aryl bromides to arylamines. *Angew. Chem., Int. Ed.* **1995**, *34*, 1348−1350.

(20) Surry, D. S.; Buchwald, S. L. Dialkylbiaryl phosphines in Pd-catalyzed amination: a user's guide. *Chem. Sci.* **2011**, *2*, 27−50.

(21) Maiti, D.; Fors, B. P.; Henderson, J. L.; Nakamura, Y.; Buchwald, S. L. Palladium-catalyzed coupling of functionalized primary and secondary amines with aryl and heteroaryl halides: two ligands suffice in most cases. *Chem. Sci.* **2011**, *2*, 57−68.

(22) Lundgren, R. J.; Stradiotto, M. Recent advances in the Buchwald−Hartwig amination reaction enabled by the application of sterically demanding phosphine ancillary ligands. *Aldrichimica Acta* **2012**, *45*, 59−65.

(23) Busacca, C. A.; Fandrick, D. R.; Song, J. J.; Senanayake, C. H. The growing impact of catalysis in the pharmaceutical industry. *Adv. Synth. Catal.* **2011**, *353*, 1825−1864.

(24) Collet, F.; Dodd, R. H.; Dauban, P. Catalytic C−H amination: Recent progress and future directions. *Chem. Commun.* **2009**, 5061−5074.

(25) Armstrong, A.; Collins, J. C. Direct azole amination: C-H functionalization as a new approach to biologically important heterocycles. *Angew. Chem., Int. Ed.* **2010**, *49*, 2282−2285.

(26) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. Recent advances in the transition metal-catalyzed twofold oxidative C−H bond activation strategy for C−C and C−N bond formation. *Chem. Soc. Rev.* **2011**, *40*, 5068−5083.

(27) Semikolenov, V. A.; Boldyreva, M. E.; Shmidt, Y. V.; Stepanov, A. G. Formation of 2,6-dimethylaniline from 2,6-dimethylphenol with catalysts obtained via anchoring colloidal palladium compounds on carbon supports. *J. Mol. Catal.* **1989**, *55*, 415−428.

(28) Shum, S. P.; Pastor, S. D.; Odorisio, P. A. Process for the preparation of tetralone imines for the preparation of active pharmaceutical compounds. Patent WO99/55686, 1999.

(29) Guinot, S. G. R.; Hepworth, J. D.; Wainwright, M. Synthesis of tertiary 1-nathylamines via the enamine. *Dyes Pigm.* **1998**, *36*, 387−393.

(30) Ishikawa, T.; Uedo, E.; Tani, R.; Saito, S. Aromatization of enamines promoted by a stoichiometric amount of palladium (II) salts: A novel method for the synthesis of aromatic amines. *J. Org. Chem.* **2001**, *66*, 186−191.

(31) Cossy, J.; Belotti, D. Aromatization of enamines promoted by a catalytic amount of Pd/C. Synthesis of aromatic Amines. *Org. Lett.* **2002**, *4*, 2557−2559.

(32) Neumann, H.; Jacobi von Wangelin, A.; Klaus, S.; Strubing, D.; Gördes, D.; Beller, M. Anilines made easily: From aldehydes to tri-, tetra-, and pentasubstituted anilines in two steps. *Angew. Chem., Int. Ed.* **2003**, *42*, 4503−4507.

(33) Horning, E. C.; Horning, M. G. Aromatization studies. IV. Palladium dehydrogenation of arylcyclohexenones to phenols. *J. Am. Chem. Soc.* **1947**, *69*, 1359−1361.

(34) Bamfield, P.; Gordon, P. F. Aromatic benzene compounds from acyclic precursors. *Chem. Soc. Rev.* **1984**, *13*, 441−488.

(35) Fu, P. P.; Harvey, R. G. Dehydrogenation of polycyclic hydroaromatic compounds. *Chem. Rev.* **1978**, *78*, 317−361.

(36) Muzart, J. One-pot syntheses of α,β-unsaturated carbonyl compounds through palladium-mediated dehydrogenation of ketones, aldehydes, esters, lactones and amides. *Eur. J. Org. Chem.* **2010**, 3779−3790.

(37) Wenzel, T. T. Cationic palladium nitro complexes as catalysts for the oxygen-based oxidation of alkenes to ketones and aldehydes to the α,β-unsaturated analogues. *J. Chem. Soc. Chem. Commun.* **1989**, 932−933.

(38) Bondon, D.; Pietrasanta, Y.; Pucci, B. Nouvelle méthode d'aromatisation de cylohexènones contenues dans des systèmes polycycliques. *Tetrahedron Lett.* **1977**, *18* (10), 821−824.

(39) Moriuchi, T.; Kikushima, K.; Kajikawa, T.; Hirao, T. Vanadium-catalyzed oxidative aromatization of 2-cyclohexenones under molecular oxygen. *Tetrahedron Lett.* **2009**, *50*, 7385−7387.

(40) Kosower, E. M.; Wu, G. S. Halogenation with copper (II). II. Unsaturated ketones. *J. Org. Chem.* **1963**, *28*, 633−638.

(41) Izawa, Y.; Pun, D.; Stahl, S. S. Palladium-catalyzed aerobic dehydrogenation of substituted cyclohexanones to phenols. *Sciences* **2011**, *333*, 209−213.

(42) Campbell, A. N.; Stahl, S. S. Overcoming the "oxidant problem": Strategies to use O₂ as the oxidant in organometallic C−H oxidation reactions catalyzed by Pd (and Cu). *Acc. Chem. Res.* **2012**, *45*, 851−863.

(43) Izawa, Y.; Zheng, C.; Stahl, S. S. Aerobic oxidative Heck/Dehydrogenation reactions of cyclohexenones: Efficient access to meta-substituted phenols. *Angew. Chem., Int. Ed.* **2013**, *52*, 3672−3675.

(44) Imahori, T.; Tokuda, T.; Taguchi, T.; Takahata, H. An alternative approach to para-C−H arylation of phenol: palladium-catalyzed tandem γ-arylation/aromatization of 2-cyclohexen-1-one derivatives. *Org. Lett.* **2012**, *14*, 1172−1175.

(45) Simon, M. O.; Girard, S. A.; Li, C. J. Catalytic aerobic synthesis of aromatic ethers from non-aromatic precursors. *Angew. Chem., Int. Ed.* **2012**, *51*, 7537−7540.

(46) Hajra, A.; Wei, Y.; Yoshikai, N. Palladium-catalyzed aerobic dehydrogenative aromatization of cyclohexanone imines to arylamines. *Org. Lett.* **2012**, *14*, 5488−5491.

(47) Girard, S. A.; Hu, X.; Knauber, T.; Zhou, F.; Simon, M. O.; Deng, G.-J.; Li, C.-J. Pd-catalyzed synthesis of aryl amines via oxidative aromatization of cyclic ketones and amines with molecular oxygen. *Org. Lett.* **2012**, *14*, 5606−5609.

(48) Xiao, F.; Liao, Y.; Wu, M.; Deng, G.-J. One-pot synthesis of carbazoles from cyclohexanones and arylhydrazine hydrochlorides under metal-free conditions. *Green Chem.* **2012**, *14*, 3277−3280.

(49) Xie, Y.; Liu, S.; Liu, Y.; Wen, Y.; Deng, G.-J. Palladium-catalyzed one-pot diarylamine formation from nitroarenes and cyclohexanones. *Org. Lett.* **2012**, *14*, 1692−1695.

(50) Leonard, N. J.; Sauers, R. R. Unsaturated amines. IX. Through bis-enamines to aromatics. *J. Org. Chem.* **1956**, *21*, 1187−1188.

(51) Rosamillia, A. E.; Scott, J. L.; Strauss, C. R. Preparation of 2- and 4-arylmethyl N-substituted and N,N-disubstituted anilines via a "green", multicomponent reaction. *Org. Lett.* **2005**, *7*, 1525−1528.

(52) Barros, M. T.; Dey, S. S.; Maycock, C. D.; Rodrigues, P. Metal-free direct amination/aromatization of 2-cyclohexenones to iodo-N-arylanilines and N-arylanilines promoted by iodine. *Chem. Commun.* **2012**, *48*, 10901−10903.

(53) Barros, M. T.; Dey, S. S.; Maycock, C. D. Metal-free synthesis of secondary arylamines: an aliphatic-to-aromatic transformation. *Eur. J. Org. Chem.* **2013**, 742−747.

(54) Sutter, M.; Dayoub, W.; Métay, E.; Raoul, Y.; Lemaire, M. Selective Synthesis of 1-O-Alkyl(poly)glycerol Ethers by Catalytic Reductive Alkylation of Carboxylic Acids with a Recyclable Catalytic System. *ChemSusChem* **2012**, *5*, 2397−2409.

(55) Sutter, M.; Dayoub, W.; Métay, E.; Raoul, Y.; Lemaire, M. 1-O-Alkyl (di)glycerol ethers synthesis from methyl esters and triglycerides

1472

dx.doi.org/10.1021/sc4002164 | ACS Sustainable Chem. Eng. 2013, 1, 1463−1473

by two pathways: catalytic reductive alkylation and transesterification/reduction. *Green Chem.* **2013**, *15*, 786−797.

(56) Sutter, M.; Sotto, N.; Raoul, Y.; Métay, E.; Lemaire, M. Straightforward heterogeneous palladium catalyzed synthesis of aryl ethers and aryl amines via a solvent free aerobic and non-aerobic dehydrogenative arylation. *Green Chem.* **2013**, *15*, 347−352.

(57) Sutter, M.; Lafon, R.; Raoul, Y.; Métay, E.; Lemaire, M. Heterogeneous palladium-catalyzed synthesis of aromatic ethers by solvent-free dehydrogenative aromatization: Mechanism, scope and limitations under aerobic and non-aerobic conditions. *Eur. J. Org. Chem.* **2013**, DOI: 10.1002/ejoc.201300485.

(58) Janin, Y. L.; Bisagni, E. A new access to 1-naphthylamines by an equivalent Semmler−Wolff reaction. *Synthesis* **1993**, 57−59.

1473

dx.doi.org/10.1021/sc4002164 | *ACS Sustainable Chem. Eng.* 2013, 1, 1463−1473