

Nickel-catalyzed cross-coupling of diarylamines with haloarenes†

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The cross-coupling reaction of diarylamines with aryl bromides/iodides can be effected by the Ni(II)–(σ -aryl) complex/ PPh_3 /NaH system, and a preliminary investigation was conducted into the mechanism of this reaction.

Nickel-catalyzed aromatic C–N coupling reactions have received intense investigations and made remarkable advances over the past decade. A considerably wide range of arylamine derivatives can be obtained from the catalytic couplings of haloarenes (primarily chloroarenes) with various types of nitrogen-containing substrates involving primary amines, secondary cyclic and acyclic amines, anilines and *N*-alkyl anilines.^{1–6} In contrast, the Ni-catalyzed *N*-arylation of diarylamines or anilines for triarylamines synthesis has been a challenging task. Triarylamines are an important class of building blocks for organic materials with unique photoelectric properties;⁷ currently their preparation depends primarily on Pd-⁸ and Cu-catalyzed⁹ C–N coupling reactions. Thus, the nickel-catalyzed triarylamines synthesis merits exploration whether from the angle of synthetic methodology or material preparation.

Our previous work displayed an interesting procedure for the Ni(II)-catalyzed *N*-arylation of bromomagnesium diarylamides for triarylamines synthesis.^{4a} However, this protocol seems to be somewhat cumbersome and complicated in manipulation since the diarylamidomagnesium bromides needed to be produced by treatment of diarylamines with the Grignard reagent and the reaction solvent THF be replaced (entirely or partly) with other solvents such as toluene or dioxane. On the other hand, a recent publication⁶ provided a single special case where a triarylamines product was afforded by the coupling of diphenylamine with 4-bromobenzophenone in the presence of Ni(II)–NHC complex as a catalyst. It was concluded from the above-mentioned outcomes that: (1) nickel-based catalytic systems would likely cause aromatic C–N couplings for triarylamines synthesis if the proper reaction conditions are chosen; and (2) more convenient, general protocols are awaiting development. Herein, we want to present a simple protocol for the nickel-catalyzed triarylamines synthesis from *N*-arylation of diarylamines through employing an easily-available Ni(II)–(σ -aryl) complex, which were previously applied to the aminations of aryl chlorides^{4b} and tosylates,^{4c} as a pre-catalyst.

The cross-coupling of diphenylamine and bromobenzene was used as a model reaction for the screening of reaction conditions. Ni(II) compounds were chosen as pre-catalysts because they were

readily available, cheaper, and convenient to manipulate due to their air-/moisture-stability. For catalytic C–N coupling reactions, bases are required to deprotonate the amine or neutralize the protons that the amine released in the reaction course. Further, considering the fact that facile reduction of the Ni(II) center may make the reaction more efficient, the use of bases possessing reducing ability should be desirable. Thus, sodium hydride, a cheap and easy-to-use base, was employed in this study as it was reported to be able to reduce Ni(II) to the catalytically active low-valent Ni species.^{3c}

As shown in Table 1, a combination of $\text{NiCl}_2(\text{PPh}_3)_2$ and PPh_3 can give triphenylamine in toluene at 120 °C upon the use of NaH as base, albeit in only 30% yield (entry 1). After some experimentation, it was found that a Ni(II)–(σ -aryl) complex, $\text{Ni}(\text{PPh}_3)_2(1\text{-naphthyl})\text{Cl}$, worked far better than $\text{NiCl}_2(\text{PPh}_3)_2$ under similar conditions, giving an excellent yield of 88% (entry 2). The difference in the catalytic activity between $\text{Ni}(\text{PPh}_3)_2(1\text{-naphthyl})\text{Cl}$ and $\text{NiCl}_2(\text{PPh}_3)_2$ might be ascribed to their different reactivity toward the reductive base NaH. Phosphine-based bidentate ligand (entry 3) was slightly inferior to triphenylphosphine, while the strongly σ -donating *N*-heterocyclic carbene (entry 4) and nitrogen-based bidentate ligand (entry 5) were ineffective. An attempt to reduce reaction temperatures from 120 °C to 100 °C led to a decreased yield (entry 6). To our surprise, elevating the reaction temperature (up to 140 °C in *m*-xylene) seemed to be very unfavorable for this reaction (entry 7). The change of reaction solvents from toluene to dioxane (entry 8) or THF (entry 9) brought a reduced yield or even no product due to the nature of the solvents and reaction temperatures. It is worth noting that almost no reaction occurred upon replacement of NaH with other bases, such as $\text{K}^+\text{O}^-\text{Bu}$ (entry 10) and $\text{Na}^+\text{O}^-\text{Bu}$ (entry 11), used normally in nickel-catalyzed C–N couplings, whether the Ni(II) or Ni(0) was utilized as the nickel source. This indicated that the use of strong bases possessing reducing ability is essential for this reaction. The role of the nickel-based catalyst system was confirmed by a control experiment (entry 12). It must be mentioned that biphenyl as a by-product was always detected, to a greater or lesser degree, in these coupling reactions involving NaH as both base and reductant. Finally, the optimized reaction conditions were set up as entry 2 in Table 1.

Next, we performed the coupling reaction between a range of haloarenes and representative diarylamines under the optimized reaction conditions. The results are summarized in Table 2. Generally, both aryl bromides and iodides are substrates suitable for this reaction, and the iodide performed a bit better than the corresponding bromide. Electron-neutral bromo- and iodobenzene were smoothly coupled with diarylamines in good to excellent yields (entries 1, 2, and 15–18); electron-rich *p*-bromotoluene gave a relatively low yield of the expected product (entries 6 and 7). The aryl chloride was resistant to the reaction

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Table 1 Screening of conditions for Ni(II)-catalyzed arylation of diphenylamine^a

Entry	[Ni] ^b (mol%)	Ligand (mol%)	Base	Solvent	Temp./°C	Yield (%) ^c
1	C-1 (5)	PPh ₃ (10)	NaH	toluene	120	30
2	C-2 (5)	PPh ₃ (10)	NaH	toluene	120	88
3	C-2 (5)	DPPE ^d (5)	NaH	toluene	120	75
4	C-2 (5)	SIPr·HCl ^e (10)	NaH	toluene	120	0
5	C-2 (5)	Phen ^f (5)	NaH	toluene	120	trace
6	C-2 (5)	PPh ₃ (10)	NaH	toluene	100	78
7	C-2 (5)	PPh ₃ (10)	NaH	<i>m</i> -xylene	140	11
8	C-2 (5)	PPh ₃ (10)	NaH	dioxane	120	60
9	C-2 (5)	PPh ₃ (10)	NaH	THF	70	trace
10	C-2 (5)	PPh ₃ (10)	KO ^t Bu	toluene	120	trace
11	Ni(0) (ca. 5) ^g	PPh ₃ (10)	NaO ^t Bu	toluene	120	trace
12	none	none	NaH	toluene	120	0

^a Reaction conditions: diphenylamine (1 equiv), bromobenzene (2 equiv), base (1.5 equiv), 12 h. ^b C-1: Ni(PPh₃)₂Cl₂; C-2: Ni(PPh₃)₂(1-naphthyl)Cl.
^c Isolated yield. ^d 1,2-Bis(diphenylphosphino)ethane. ^e 1,3-Bis(2,6-diisopropylphenyl)-4,5-dihydroimidazolium chloride. ^f 1,10-Phenanthroline. ^g The Ni(0) species was *in situ* generated from Ni(PPh₃)₂Cl₂ and CH₃MgBr following the literature procedure (see ref. 1).

conditions (entry 3). Thus, a selective amination of 4-bromo-1-chlorobenzene (entry 4) and 3-bromo-1-chlorobenzene (entry 5) may be carried out. The nature of electron-withdrawing groups on haloarenes affected the reaction substantially. For example, the bromoarene bearing the inert chlorine-aryl bond could offer acceptable yields (entries 4 and 5). Rather, those containing the carbonyl group, such as 4-bromobenzophenone (entry 12), 4-bromobenzaldehyde (entry 13) and 4-bromobenzoate (entry 14), provided only small amounts of or no desired product, although the starting bromides were found to be consumed completely. This might be because the carbonyl group may capture the electrons resulting from the NaH-related electron transfer process to form the carbonyl radical anion,¹⁰ leading to a failure in the reduction of the Ni(II) into the catalytically active low-valent Ni species. On the other hand, this reaction is very sensitive to the steric hindrances of both types of substrates. For example, *o*-methyl-substituted haloarenes (entries 8–10) furnished far lower yields than those without ortho-substituents; a similar outcome was observed in the case of 1-bromonaphthalene (entry 11). And unhindered 4,4'-dimethyldiphenylamine with the electron-donating group provided high yields similar to diphenylamine (entries 15 and 16), but the yields rapidly decreased from diphenylamine, phenyl(2-naphthyl)amine to phenyl(1-naphthyl)amine with increasing the steric bulk of amine substrates (entry 1 *versus* entry 17; and entry 2 *versus* entry 18 *versus* entry 19).

It was found that this reaction is quite different from most of the nickel-catalyzed aromatic C–N couplings reported previously. For instance, chloroarenes were inert in the reaction; the homo-coupling of bromo-/iodoarenes producing biaryls occurred as a major side reaction to a greater or lesser degree in almost all cases; the conversion efficiencies increased with the increase of the concentration of bromo-/iodoarenes; and the reaction proceeded only in the presence of strong bases with reducing ability such as sodium hydride, the Grignard reagent or the organolithium reagent. To discern the mechanism of the reaction, we conducted a stoichiometric reaction of sodium diphenylamide with

Ni(II)–(σ-aryl) complexes¹¹ that may be regarded as the oxidative adducts of haloarenes to Ni(0) as shown in eqn (1). As a result, no triarylamine product was detected. Thus, it should be safe to rule out the mechanism to follow an usual Ni(0)–Ni(II) cycle for this nickel-catalyzed triarylamine synthesis.

It was presumed that the catalytically active species might be the Ni(I) species in this reaction. The Ni(I) may be generated *in situ* by one-electron transfer of the *in situ*-generated Ni(0) species to the haloarene¹² following the reaction steps as shown in Scheme 1. Combining previous studies¹³ with our experimental results, a plausible mechanism is proposed that might follow a catalytic cycle of the Ni(I)–Ni(III) shuttle involving sequential oxidative addition, transmetalation and reductive elimination (Scheme 2). This conclusion may partly explain the reasons why aryl chlorides do not react under the conditions and there always existed a considerable amount of biaryl by-product. The rate-determining step of the reaction is unclear at present.

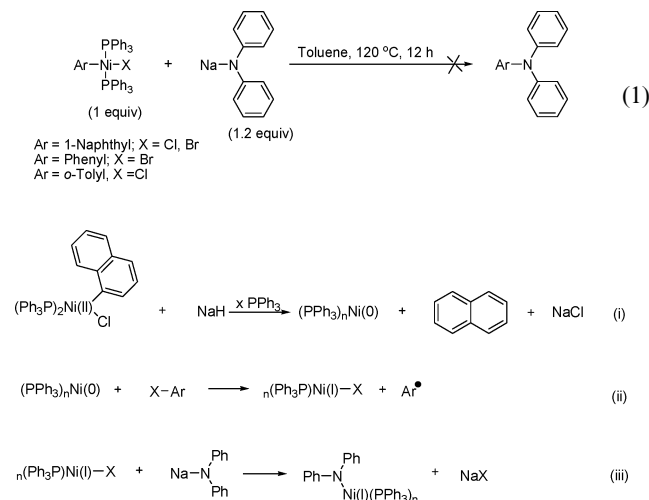
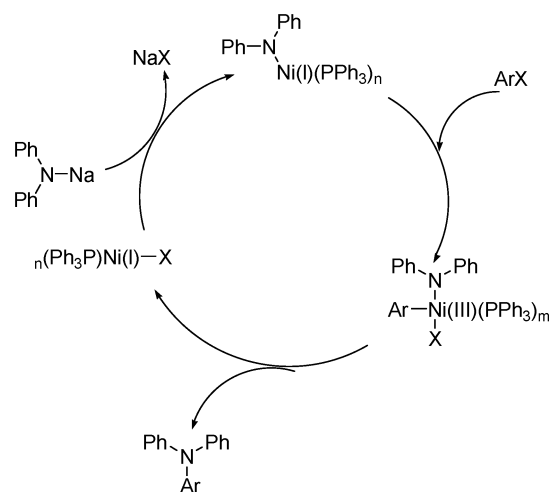
**Scheme 1** A proposed route to *in situ* generation of the catalytically active Ni(I) species.

Table 2 Nickel-catalyzed arylation of diarylamines with haloarenes^a

Entry	Aryl bromide (iodide)	Diarylamine	Isolated yield (%)
1			88
2			90
3			no reaction
4			60
5			63
6			65
7			68
8			45
9			40
10			47
11			35
12			23 ^b
13			0 ^b
14			0 ^b
15			85
16			87
17			61
18			63
19			29

^a Reaction conditions: diarylamine (1 equiv), haloarenes (1.5–2 equiv), NaH (1.5 equiv), 120 °C, 12 h. ^b Aryl bromide was consumed completely.

active Ni(I) species

**Scheme 2** A proposed mechanism for the arylation of diarylamines with bromo-/iodoarenes catalyzed by the Ni(II)–(σ-aryl) complex/PPh₃/NaH system.

In conclusion, we have once again demonstrated the possibility of the nickel-catalyzed aromatic C–N coupling for triarylamine synthesis. A preliminary investigation suggested that the mechanism of this reaction might be different from that of the normal nickel-catalyzed C–N couplings following a catalytic cycle of the Ni(0)–Ni(II) shuttle. Meanwhile, this simple, practical protocol for triarylamine synthesis functions, to a certain extent, as a complement or alternative to the corresponding palladium and copper catalyses, and further enhances the utility of Ni(II)–(σ-aryl) complexes as catalysts for the cross-coupling reactions. Studies are underway in our laboratory to improve the reaction conditions for expansion of the substrate scope as well as to detail information on the mechanism of this reaction.

Experimental section

General procedure for the nickel-catalyzed arylation of diarylamine with aryl halide

An oven-dried 50-mL three-necked flask was charged with sodium hydride (120 mg of 60% NaH in white oil, 3 mmol), Ni(PPh₃)₂(1-naphthyl)Cl (74 mg, 5 mol % relative to diarylamine), and PPh₃ (52 mg, 10 mol% relative to diarylamine). The diarylamine (2 mmol) and the aryl halide (3–4 mmol) were added at this time if solid. The flask was evacuated and backfilled with nitrogen, with the operation being repeated twice. Dried toluene (10 mL) was added *via* syringe, followed by the aryl halide (4 mmol) if liquid. The reaction mixture was heated in an oil bath at 120 °C for 12 h. The reaction mixture was allowed to cool to room temperature, quenched with H₂O (20 mL), and filtered through a pad of silica gel. The organic layer was separated and the aqueous phase extracted with toluene (20 mL × 2). Then the combined organic phases were dried over anhydrous MgSO₄ and filtered. The filtrate was evaporated under reduced pressure and the residue purified by column chromatography on silica gel with petroleum ether to afford the analytically pure product in the isolated yields indicated in Table 2.

Triphenylamine (Table 2, entry 1)

According to the general procedure, sodium hydride (120 mg of 60% NaH in white oil, 3 mmol), Ni(PPh₃)₂(1-naphthyl)Cl (74 mg, 5 mol %), PPh₃ (52 mg, 10 mol%), diphenylamine (338 mg, 2 mmol), and bromobenzene (628 mg, 4 mmol) were transformed into the product as a white solid (430 mg, 88%); mp 127–128 °C (lit.,¹⁴ mp 127 °C). ¹H NMR (CDCl₃, 400 MHz): δ 7.01 (t, *J* = 7.6 Hz, 3H), 7.10 (d, *J* = 7.6 Hz, 6H), 7.25 (t, *J* = 7.6 Hz, 6H); MS (EI): *m/z* 245 (M⁺). CAS Number: 603-34-9.

A typical experiment to study the reaction of Ni(II)–(σ-aryl) complex and sodium diphenylamide

Under N₂ atmosphere, to a solution of diphenylamine (1.2 mmol, 203 mg) in toluene (5 mL) was added sodium hydride (48 mg of 60% NaH in white oil, 1.2 mmol) at room temperature and the mixture was stirred for 1 h. Then the nickel(II)–(σ-aryl) complex (1 mmol) was added to the reaction mixture, followed by heating in an oil bath at 120 °C for 12 h. The reaction mixture was worked up *via* the normal procedure and examined by TLC and GC-MS techniques.

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