

with aryl and heteroaryl halides and sulfonates,<sup>[2]</sup> and also with alkenyl halides.<sup>[3]</sup> With regard to the nitrogen coupling partner, most NH functional groups can participate in this coupling reaction, including C=N-containing species such as benzophenone imine,<sup>[4]</sup> and sulfoximines.<sup>[5]</sup> However, despite the intense development of this reaction in the recent years, the direct preparation of *N*-substituted aldimines by a cross-coupling protocol has not been described yet, probably as a result of the instability of the required NH aldimines. Nevertheless, the one-step transformation of bromides into aldimines is a very interesting reaction indeed, as imines are very versatile starting materials in synthetic organic chemistry, and especially in heterocyclic chemistry. Moreover, aldimines can be hydrolyzed under very mild conditions, therefore the direct synthesis of imines might be a new alternative for the introduction of the -NH<sub>2</sub> group.<sup>[6]</sup>

Herein we describe the one-step synthesis of aldimines and of 1- and 2-azadienes from aryl and alkenyl bromides and introduce the readily available *N*-trialkylsilyl imines as surrogates for the unstable NH-aldimines in palladium-catalyzed C–N bond-forming reactions.

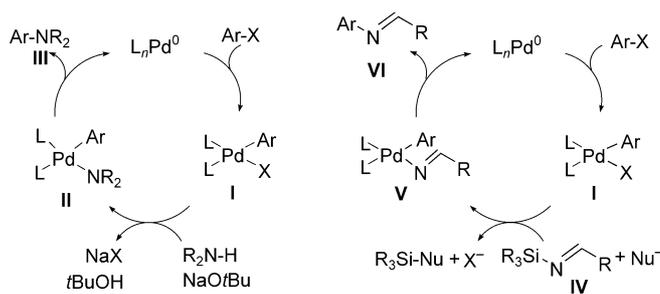
The palladium-catalyzed aryl amination involves three fundamental steps<sup>[7]</sup> (Scheme 1, left): 1) oxidative addition of the aryl halide to a Pd<sup>0</sup> complex to form aryl–palladium–halide complex **I**; 2) transformation of **I** into amido complex

## Cross-Coupling

### *N*-Trialkylsilylimines as Coupling Partners for Pd-Catalyzed C–N Bond-Forming Reactions: One-Step Synthesis of Imines and Azadienes from Aryl and Alkenyl Bromides\*\*

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The palladium-catalyzed amination of aryl halides, known as the Buchwald–Hartwig reaction, has become a widely employed method in recent years for the synthesis of aryl amines.<sup>[1]</sup> The broad scope of this C–N bond-forming reaction allows its application with a variety of both reactants, the halide and the nitrogen source. In fact, very efficient catalytic combinations have been uncovered for the coupling of amines



**Scheme 1.** Left: Simplified mechanism of the palladium-catalyzed aryl amination. Right: Proposed mechanism for a cross-coupling reaction involving an *N*-trialkylsilyl imine.

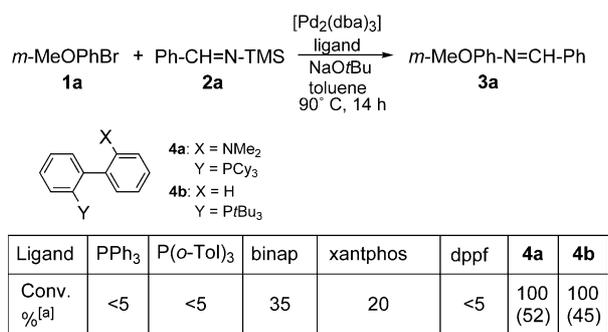
**II** (this step requires the presence of a base to cleave the N–H bond); 3) reductive elimination to form the aryl amine **III** and to regenerate the Pd<sup>0</sup> catalyst. A similar catalytic cycle could be proposed by replacing the amine with an *N*-trialkylsilyl imine **IV** (Scheme 1, right). In such a case, a proper nucleophilic additive is required to promote the cleavage of the N–Si bond and to form the imido complex **V**.<sup>[8]</sup> We decided to explore this possibility, which would lead directly to aldimines **VI** from aryl or alkenyl bromides.

In an initial set of experiments, we studied the reaction of *m*-bromoanisole (**1a**) with the *N*-trimethylsilylimine **2a**<sup>[9]</sup> (Scheme 2) and chose the Pd<sup>0</sup>–binap catalytic system. The reactions were carried out in toluene at 90 °C with Pd (1 mol%) in the presence of different additives. Only the formation of the cross-coupling imine **3a** was observed, although with low conversion (35%), in the reaction carried out in the presence of NaOtBu. Other basic reagents such as NaOMe and triethylamine furnished unaltered starting

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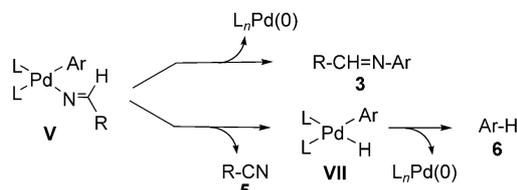
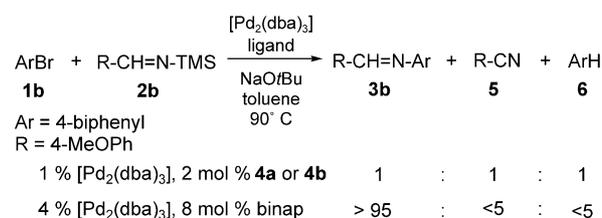
**Scheme 2.** Influence of the ligand in the coupling of *N*-trimethylsilylbenzaldimine (**2a**) with 3-bromoanisole (**1a**) in the presence of [Pd<sub>2</sub>(dba)<sub>3</sub>]. Reaction conditions: **1a** (1 equiv), **2a** (1.1 equiv), NaOtBu (1.4 equiv), [Pd<sub>2</sub>(dba)<sub>3</sub>] (1 mol%), ligand (2 mol%), toluene (2 mL/mmol), 90°C, 14 h. dba = dibenzylideneacetone, binap = 2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl, xantphos = 9,9-dimethyl-4,5-bis-(diphenylphosphanyl)xanthene, dppf = 1,1'-bis(diphenylphosphanyl)ferrocene. [a] Yield of isolated **3a** when **4a** and **4b** were used are indicated in parentheses.

materials. No reaction was observed either with CsF in toluene (probably as a result of solubility problems),<sup>[10]</sup> and phase-transfer catalysts such as methyltribenzylammonium chloride and tetrabutylammonium fluoride resulted in the decomposition of the silylimine with no coupling product being formed.<sup>[11]</sup>

The same reaction in the presence of NaOtBu was then studied with a set of different ligands. Only with biphenyl ligands **4a** and **4b** was complete conversion achieved (Scheme 2).<sup>[12]</sup> However, the yield of pure distilled material did not exceed 52%.

In a different series of experiments with the 4-bromobiphenyl **1b** and silylimine **2b** (Scheme 3), it was observed that the reaction with ligands **4a** and **4b** provided a mixture of coupling product **3b**, 4-methoxybenzotrile **5**, and biphenyl **6** in a nearly 1:1:1 ratio. This result could be explained by a competing catalytic cycle in which β-elimination in complex **V** would release nitrile **5** and generate hydride complex **VII**. Finally, reductive elimination would give rise to the dehalogenated aromatic hydrocarbon **6** and regenerate the palladium catalyst.<sup>[13,14]</sup> Apparently, with biphenyls **4** as ligands, both reaction pathways occur to a similar extent. Nevertheless, by using binap and increasing the catalyst loading from 1 to 4 mol%, complete conversions were possible, and interestingly, less than 5% β-elimination was observed.

The reaction was generalized to a range of aryl bromides and silylimines. As represented in Table 1, the coupling proceeds with good to



**Scheme 3.** Influence of the ligand on the ratio of reductive elimination vs β-elimination.

quantitative yields and tolerates electron-donating and -withdrawing groups and some heterocyclic motifs (Table 1, entries 7–9) in both coupling partners. Interestingly, the same reaction allows the synthesis of aldimines **3**, 1-azadienes **7**, 2-azadienes **8**, and even azatrienes **9**, depending on the structure of the coupling partners.

The reaction with vinyl bromides (Table 1, entries 12–14), which constitutes a novel synthesis of electronically neutral 2-azadienes **8** and 2-azatriene **9**, which are very versatile reagents in heterocycloaddition reactions.<sup>[15]</sup> In this case, the use of ligand **4a** is preferred (method B), as no β-elimination products were formed. Owing to the higher activity of this catalytic system, complete conversions are possible in much shorter times and with lower catalyst loadings.

In summary, we have introduced *N*-trialkylsilylimines **2** as very efficient synthetic equivalents of the unstable and

**Table 1:** Coupling of silylimines **2** with aryl and alkenyl halides **1**.

| Entry | $\text{R}^1\text{Br} + \text{R}^2\text{-CH=N-TMS} \xrightarrow[\text{NaOtBu, toluene, 90}^\circ\text{C}]{[\text{Pd}_2(\text{dba})_3], \text{binap or } \mathbf{4a}}$ |                 | Product   | Method <sup>[a]</sup> | t [h] <sup>[b]</sup> | Yield [%] <sup>[c]</sup> |
|-------|--|-----------------|-----------|-----------------------|----------------------|--------------------------|
|       | <b>1</b>   | <b>2</b>        |           |                       |                      |                          |
| 1     | <i>m</i> -MeOPh  | <i>p</i> -MeOPh | <b>3c</b> | A                     | 14                   | 97                       |
| 2     | <i>p</i> -ClPh   | <i>p</i> -MeOPh | <b>3d</b> | A                     | 14                   | 86                       |
| 3     | <i>m</i> -CNPh   | <i>p</i> -MeOPh | <b>3e</b> | A                     | 20                   | 79                       |
| 4     | <i>o</i> -EtPh   | <i>p</i> -MeOPh | <b>3f</b> | A                     | 14                   | 95                       |
| 5     | <i>m</i> -CNPh   | <i>p</i> -ClPh  | <b>3g</b> | A                     | 14                   | 76                       |
| 6     | <i>o</i> -EtPh   | <i>p</i> -ClPh  | <b>3h</b> | A                     | 14                   | 96                       |
| 7     | 3-Py   | <i>p</i> -ClPh  | <b>3i</b> | A                     | 20                   | 86                       |
| 8     | <i>o</i> -EtPh   | 2-Furyl         | <b>3j</b> | A                     | 14                   | 92                       |
| 9     | <i>p</i> -CF <sub>3</sub> Ph   | 2-Furyl         | <b>3k</b> | A                     | 14                   | 90                       |
| 10    | <i>p</i> -ClPh   | Ph-CH=CH-       | <b>7a</b> | A                     | 14                   | 95                       |
| 11    | <i>m</i> -MeOPh  | Ph-CH=CH-       | <b>7b</b> | A                     | 20                   | 86                       |
| 12    | Ph-CH=CH-  | <i>p</i> -ClPh  | <b>8a</b> | B                     | 2                    | 92                       |
| 13    | Ph-CH=CH-  | <i>p</i> -MeOPh | <b>8b</b> | B                     | 3                    | 90                       |
| 14    | Ph-CH=CH-  | Ph-CH=CH-       | <b>9</b>  | B                     | 3                    | 93                       |

[a] Method A: **1** (1 equiv), **2** (1.2 equiv), NaOtBu (1.4 equiv), [Pd<sub>2</sub>(dba)<sub>3</sub>] (4 mol%), BINAP (8 mol%), toluene (2 mL/mmol), 90°C. Method B: **1** (1 equiv), **2** (1.2 equiv), NaOtBu (1.4 equiv), [Pd<sub>2</sub>(dba)<sub>3</sub>] (2 mol%), **4a** (4 mol%), toluene (2 mL/mmol), 90°C. [b] Reaction times were not optimized. [c] Yields of isolated product on a 0.5-mmol scale.

unavailable NH aldimines in palladium-catalyzed cross-coupling reactions. The coupling with aryl bromides allows the one-step synthesis of aldimines, and the reaction with vinyl bromides gives rise to neutral 2-azadienes with excellent yields. Given the easy availability of structurally diverse and functionalized *N*-trialkylsilyl imines<sup>[9,16]</sup> and the good yields of the coupling reaction, we believe that this transformation may be very useful in heterocyclic chemistry and diversity-oriented organic synthesis. Moreover, these results open the door for the incorporation of *N*-trialkylsilyl imines in other types of metal-catalyzed cross-coupling processes.

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