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# Palladium/P($t$-Bu)$_3$-catalyzed synthesis of *N*-aryl azoles and application to the synthesis of 4,4′,4′′-tris(*N*-azolyl)triphenylamines

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## Abstract

Palladium/P($t$-Bu)$_3$ catalyzed the coupling of aryl halides with azoles such as pyrrole, indole, and carbazole, effectively. $K_2CO_3$ and $Rb_2CO_3$ worked very well as bases, whereas $Cs_2CO_3$ and *t*-BuONa gave only trace yields of products. Triazolyl compounds such as TCTA were also synthesized. © 2000 Elsevier Science Ltd. All rights reserved.

*Keywords:* amination; palladium catalysts; phosphine; azoles; arylation.

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*N*-Aryl azoles have attracted attention as hole transport molecules for organic light-emitting diodes (LEDs)[1] and biologically active compounds.[2] *N*-Arylation of azole compounds was carried out by metal-mediated reactions such as the Ullmann coupling,[1,3] aromatic nucleophilic substitution using KF/$Al_2O_3$,[4] $Cr(CO)_3$ complexed haloarenes as substrates,[2] and Pd- and Cu-catalyzed arylation.[5] However, the employment of aprotic polar solvents such as DMF and a stoichiometric amount of $Cr(CO)_3$, and harsh reaction conditions diminish the applicability of these methods, especially for large-scale production. On the other hand, palladium/DPPF-catalyzed *N*-arylation of azoles with aryl bromides using $Cs_2CO_3$ or *t*-BuONa was recently reported.[6] The reaction with electron-poor aryl bromides took place in the presence of 1 mol% of $Pd(OAc)_2$, whereas catalytic activity was low on reaction with bromobenzene and electron-rich aryl bromides requiring 5 mol% of palladium.

We showed that palladium/P($t$-Bu)$_3$ was highly active and selective in *N*-arylation of amines with aryl halides.[7] We also disclosed tin-mediated synthesis of *N*-aryl azoles using the same catalyst.[8] Although high catalytic activity (0.25 mol% of Pd per halogen atom of aryl halides) and the synthesis of elaborate *N*-aryl azoles were attained, the employment of a stoichiometric amount of a tin compound is a drawback. We herein report highly efficient tin-free *N*-arylation of azoles with aryl halides using palladium and P($t$-Bu)$_3$.

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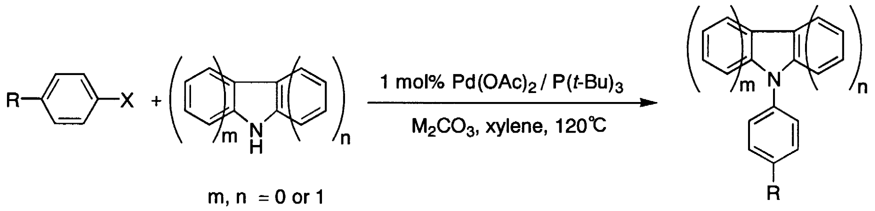
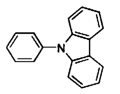
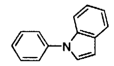
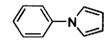
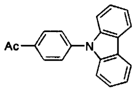
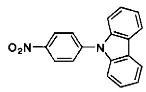
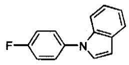
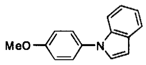
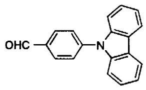


(1)

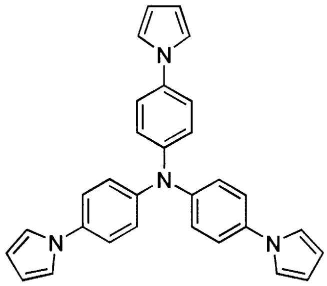
Table 1
Palladium-catalyzed synthesis of *N*-aryl azoles[a]

| Entry | Aryl Halide | | Azole | Base | Time / h | Product | Yield[b] / % |
|---|---|---|---|---|---|---|---|
| | R | X | | | | | |
| 1 | H | Br | Carbazole | $Na_2CO_3$ | 20 |  | 15[c] |
| 2 | H | Br | Carbazole | $K_2CO_3$ | 8 | | >95[c] |
| 3 | H | Br | Carbazole | $Rb_2CO_3$ | 3 | | >95[c] |
| 4 | H | Br | Carbazole | $Cs_2CO_3$ | 8 | | <5[c] |
| 5 | H | Br | Carbazole | *t*-BuONa | 8 | | <5[c] |
| 6 | H | Br | Indole | $Rb_2CO_3$ | 4 |  | 96 |
| 7 | H | Br | Pyrrole | $Rb_2CO_3$ | 6 |  | 70 |
| 8 | Ac | Br | Carbazole | $K_2CO_3$ | 9 |  | 89 |
| 9 | $NO_2$ | Br | Carbazole | $Rb_2CO_3$ | 5 |  | 65 |
| 10 | F | Br | Indole | $K_2CO_3$ | 24 |  | 78 |
| 11 | MeO | Br | Indole | $Rb_2CO_3$ | 24 |  | 75 |
| 12 | CHO | Cl | Carbazole | $K_2CO_3$ | 6 |  | 71[d] |

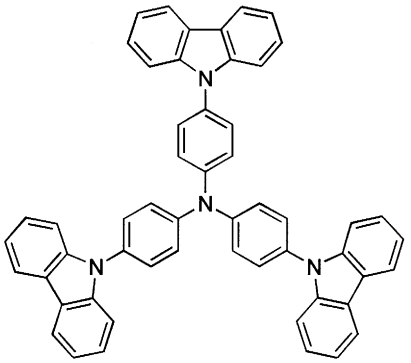
[a] The reaction was conducted in the presence of 1 mol% $Pd(OAc)_2$ / 3 mol% P(*t*-Bu)$_3$, 1.1 equiv of aryl halide, 1 equiv of azole and 3 equiv of base in *o*-xylene at 120℃.
[b] Isolated yield by column chromatography on $Al_2O_3$ (hexane/AcOEt), unless otherwise noted.
[c] Determined by GC analysis using triphenylamine as internal standard.
[d] Isolated by washing with methanol of the crude reaction mixture at 60℃.

Palladium-catalyzed synthesis of *N*-aryl azoles is summarized in Eq. (1) and Table 1. Reaction of bromobenzene with carbazole was examined with various kinds of bases. *N*-Phenylation proceeded using carbonates, and the yields increased in the order of increase of basicity (runs 1–3). However, use of $Cs_2CO_3$ gave no substantial amount of the product, nor did *t*-BuONa (runs 4 and 5). This outcome shows a sharp contrast to DPPF-ligated palladium catalyst, which allows the use of $Cs_2CO_3$ and *t*-BuONa.[6] In our catalytic system, $K_2CO_3$ and $Rb_2CO_3$ worked very well. The reason is still unclear but the employment of the stronger bases may cause formation of a significant amount of metal carbazolyl, which is assumed to deactivate the palladium catalyst. Although employing 1 equivalent of a base gave an acceptable yield, the reaction was accelerated by using 3 equivalents of the base. *N*-Phenylation of indole and pyrrole proceeded similarly (runs 6 and 7). Reactions of aryl halides bearing substituents with azoles were investigated. Both electron-poor and -rich aryl halides were converted into *N*-aryl azoles in good to high yields (runs 8–11). This electron-rich catalyst can also couple *p*-chlorobenzaldehyde with carbazole (run 12).

As described above, $K_2CO_3$ and $Rb_2CO_3$ promoted good activity in this reaction and the use of $K_2CO_3$ is more preferable practically. Therefore, we examined the synthesis of triazole derivatives such as TCTA in the presence of 3 mol% of $Pd(OAc)_2$ and 9 equivalents of $K_2CO_3$ to aryl trihalide. Reactions of 3 equivalents of pyrrole and carbazole with tri(4-bromophenyl)amine were carried out in *o*-xylene at 120°C for 24 h to afford 4,4′,4′′-tris(*N*-pyrrolyl)triphenylamine (TPTA, **1**)[9] in 65% yield and 4,4′,4′′-tris(*N*-carbazolyl)triphenylamine (TCTA, **2**)[1a,10] in 59% yield, respectively. Thus, the catalytic system consisting of palladium and P(*t*-Bu)$_3$ can provide a more efficient and practical synthetic method of *N*-aryl azoles.



**1**



**2**

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8. Watanabe, M.; Nishiyama, M.; Yamamoto, T.; Koie, Y. *Speciality Chemicals* **1998**, *18*, 445-450.
9. Compound **1** was isolated by column chromatography on $SiO_2$ (hexane:AcOEt). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$=6.32 (d, *J*=2.0 Hz, 6H), 7.04 (d, *J*=2.0 Hz, 6H), 7.13 (d, *J*=6.1 Hz, 6H), 7.29 (d, *J*=6.1 Hz, 6H).
10. Compound **2** was isolated by reprecipitation from THF–MeOH. In Ref. 1a, **2** was prepared from triiodotriphenylamine with carbazole by the Ullmann protocol.