Arylchlorogermanes/TBAF/“Moist” Toluene: A Promising Combination for Pd-Catalyzed Germyl-Stille Cross-Coupling

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ABSTRACT

The trichlorophenyl-, dichlorodiphenyl-, and chlorotriphenylgermanes undergo Pd-catalyzed cross-couplings with aryl bromides and iodides in the presence of TBAF in toluene with addition of the measured amount of water. One chloride ligand on the Ge center allows efficient activation by fluoride to promote transfer of one, two, or three phenyl groups from the organogermane precursors.

The Pd-catalyzed cross-coupling of organogermanes has thus far received much less attention than the couplings involving organostannanes and organosilanes. This is due to the lower reactivity of tetracoordinated organogermanium species, the less developed syntheses of vinyl/aryl germanyl derivatives, and the higher cost of germanium relative to silicon. The carbagermatranes 1, with internal coordination of nitrogen to germanium, were the first examples of reactive tetracoordinated germanes applied to Pd-catalyzed cross-coupling reactions with aryl bromides (Figure 1). The oxagermatranes 2 were found to be more efficient than carbagermatranes and triethoxygermanes. Fluoride-promoted couplings with aryltr(2-furyl)germanes 3 and NaOH-activated couplings with

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Figure 1. Organogermanes utilized in Pd-catalyzed couplings.
arylgermanium trichlorides8 or their hydrolyzed and stable sesquioxide alternatives9 were also reported. The bis-(2-naphthylmethyl)arylgermanes 3 were developed as photochemically activated arylgermanes for the synthesis of biaryls.10,11 The vinyl tris(trimethylsilyl)germanes 4 were employed as transmetalation reagents in “ligand- and fluoride-free” coupling reactions with halides under oxidative conditions (H2O2).12,13 The (α-fluoro)vinyl germanes 5 gave access to fluoroalkanes,14 although application of (α-fluoro)vinyl stannanes and silanes to couplings has had limited success.15,16 Recently, couplings of vinyltributylgermanes with aryl halides were found to occur more efficiently under Heck than Stille conditions to give preferentially Z-alkenes.17

In general, couplings with organogermaines appear to be promoted by: (i) activation of germanium by internal coordination/chelation,4,5,17 (ii) formation of the hypervalent species with germanium–oxygen bonds;7–9,13 and (iii) the presence of two labile heteroatom ligands (e.g., Cl or F) on Ge atom.10,11 Herein, we report that chlorophenylgermanes with at least one labile chloride ligand are activated by fluoride in “moist” toluene to allow efficient transfer of up to three phenyl groups from germane precursors during Pd-catalyzed coupling reactions with aryl halides. Treatment of PhGeMe2Cl 6 with 1-iodonaphthalene in the presence of tetrabutylammonium fluoride (TBAF) and tris(dibenzylideneacetone)dipalladium(0) [Pd2(dba)3] in toluene gave cross-coupling product 7a in addition to the binaphthyl homocoupling byproduct 8a (Table 1). The amount of TBAF was found to be crucial for the successful coupling (entries 1–5). At least 4 equiv of TBAF were required to produce 7a in maximum yield. Other Pd catalysts afforded 7a in lower yields and a decreased ratio of 7a to 8a (entries 6–7). Replacing 1 M TBAF/THF solution with neat TBAF•3H2O also gave product 7a (entry 8). Coupling in the presence of Me2NF, CsF, or NH3 instead of TBAF failed to produce 7a. The reaction also proceeded successfully at 80 °C (80%; 10:1) as well as at reflux in benzene (90%; 10:1), requiring 12 h for the best results (entry 4).

Toluene was the obvious solvent choice since attempts in DMSO (5%, 110 °C) or THF at reflux (0%) or dioxane at reflux (59%; 3:1) failed or afforded 7a in lower yields. Higher yield for the coupling in dioxane than in THF may be attributable to the increased temperature of the reaction as well the difference in dielectric constant (7.58 for THF as compared to dioxane (2.21) and toluene (2.15)).18 Bases such as NaOH [Pd(OAc)2; dioxane/H2O, 2:1] or KOSiMe3 [Pd2(dba)3, toluene], instead of TBAF, failed or were less efficient in promoting couplings.

We next examined couplings of Ph2GeCl2 9 or Ph3GeCl 10 with iodonaphthalene. Treatment of 9 with 1.1 equiv of iodide and 7 equiv of TBAF gave 7a (Table 2, entry 1). Coupling of 9 with 2.2 equiv of iodonaphthalene also resulted in total consumption of iodide to afford 7a and 8a (entry 2). Interestingly, couplings in toluene with addition of the measured amount of water (1 M TBAF/THF/H2O; ~1:5 M/M) gave a higher yield of 7a with a superior ratio of 7a:8a (entries 3 vs 1 and 4 vs 2). An investigation of the coupling reactions with different amounts of water, revealed that addition of 100 μL of H2O (~40 equiv) gave optimal yields (entry 10). Two phenyl groups were efficiently transferred in the presence of excess iodide (e.g., 89%, entry 4; yield is based upon two phenyl groups transferring from the chlorogermane reagent 9). Halides are often used in couplings as limiting reagents to reduce formation of homocoupling byproducts and the yields are based on the halide components unlike herein.

Couplings of 10 with 1.1, 2.2, or 3.3 equiv of iodonaphthalene proceeded with efficient transfer of up to three phenyl groups to give 7a (entries 5–10). [See Supporting Information for the GC/MS of the crude reaction mixture between 9 or 10 with iodonaphthalene (entries 4 and 10)] Again, yields and 7a:8a ratios increased when wet toluene was used. Atom-efficient Stille cross-couplings of Ar2Sn with aryl halides, where all four substituents on tin participate in the

### Table 1. Effect of Various Reaction Parameters on the Efficiency of Cross-Coupling of Chlorodimethylgermane 6 with 1-Iodonaphthalene

<table>
<thead>
<tr>
<th>entry</th>
<th>Pd</th>
<th>TBAF (M)</th>
<th>7a yield (%)</th>
<th>ratio (7a:8a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd[dba]3</td>
<td>1.0</td>
<td>19</td>
<td>1:1</td>
</tr>
<tr>
<td>2</td>
<td>Pd[dba]3</td>
<td>2.0</td>
<td>61</td>
<td>9:1</td>
</tr>
<tr>
<td>3</td>
<td>Pd[dba]3</td>
<td>3.0</td>
<td>79</td>
<td>17:1</td>
</tr>
<tr>
<td>4</td>
<td>Pd[dba]3</td>
<td>4.0</td>
<td>93&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20:1</td>
</tr>
<tr>
<td>5</td>
<td>Pd[dba]3</td>
<td>5.0</td>
<td>94</td>
<td>12:1</td>
</tr>
<tr>
<td>6</td>
<td>Pd[OAc]2</td>
<td>4.0</td>
<td>58</td>
<td>5:2</td>
</tr>
<tr>
<td>7</td>
<td>Pd[PPh4]3</td>
<td>4.0</td>
<td>5</td>
<td>2:1</td>
</tr>
<tr>
<td>8</td>
<td>Pd[dba]3</td>
<td>4.0&lt;sup&gt;c&lt;/sup&gt;</td>
<td>70</td>
<td>6:1</td>
</tr>
</tbody>
</table>

*Couplings were performed on 0.14 mmol scale of 6 (0.04 M) with 1.1 equiv of iodonaphthalene and 0.09 equiv of Pd catalyst. *Commercial 1 M THF solution containing 5% of water, unless otherwise noted. *Determined by GC-MS of the crude reaction mixture. *Isolated yield. After 4 h, 49% (8:1); 8 h, 78% (15:1). *With TBAF•3H2O.
carbon–carbon bond formation, are known.\textsuperscript{19,20} Also, vinylpolysiloxanes were shown to transfer each of their vinyl groups during Pd-catalyzed couplings with aryl and alkenyl iodides in the presence of TBAF.\textsuperscript{21} However, attempts to induce multiple transfer of the phenyl group during fluoride-promoted couplings of (allyl)\textsubscript{2}Ph\_\textsubscript{2}Si (x = 1 or 2) with aryl halides failed.\textsuperscript{22}

Couplings of 9 or 10 with other aryl, alkenyl, and heterocyclic iodides and bromides (using 2.2 or 3.3 equiv of halide) promoted by TBAF/H\textsubscript{2}O were presented in Table 3 (entries 1–14). Reactions of germanes 9 or 10 with reactive 4-idoacetophenone produced 7d in low yields in addition to large quantities of the reductive homocoupling byproduct 8d. However, coupling of the less reactive 4-bromoacetophenone at higher temperature (115 °C) resulted in better yields and improved 7d:8d ratios (entries 5 vs 4 and 12 vs 11). Treatment of PhGeCl\textsubscript{3} 11 with halides and TBAF/toluene or wet toluene also afforded coupling products 7 (entries 15–22), although it has been reported that fluoride ion did not promote the couplings of PhGeCl\textsubscript{3} with aryl halides.\textsuperscript{8} It appears that reactivity of the chlorogermanes increases with the number of halogen ligands on the Ge center (10 < 9 < 11). As expected,\textsuperscript{11} coupling attempts with Ph\textsubscript{2}Ge failed reinforcing the needs for at least one labile heteroatom ligand at the Ge center. The necessity of two halogen ligands had been proposed for nucleophilic activation by F\textsuperscript{−} or OH\textsuperscript{−} ions.\textsuperscript{11}

TBAF most likely facilitates the coupling by generating \textsuperscript{\textsuperscript{\textsuperscript{a}} method A: Couplings were performed on 0.14 mmol scale of germane (0.04 M) with Pd\textsubscript{2}(dba)\textsubscript{3} (0.09 equiv) and 7 equiv of TBAF (1 M/THF). Method B: as in Method A with addition of H\textsubscript{2}O (100 \mu l). \textsuperscript{\textsuperscript{\textsuperscript{a}}} Based upon transferring two phenyl groups from 9 or three phenyl groups from 10. Determined by GC–MS of the crude reaction mixture (isolated yields in parentheses). \textsuperscript{\textsuperscript{\textsuperscript{a}}} 26% and 31% with 6 and 8 equiv of TBAF. \textsuperscript{\textsuperscript{\textsuperscript{a}}} 11% and 14% with 6 and 8 equiv of TBAF. \textsuperscript{\textsuperscript{\textsuperscript{a}}} 57% (3.8:1) with 50 \mu l H\textsubscript{2}O; 82% (7:1) with 150 \mu l H\textsubscript{2}O.

\begin{table}[h]
\begin{center}
\begin{tabular}{|c|c|c|c|c|}
\hline
entry & germane & RX (equiv) & method & \textsuperscript{yield(\%)} & ratio (7a:8a) \\
\hline
1 & 9 & 1.1 & A & 32 (30) & 2.7:1 \\
2 & 9 & 2.2 & A & 58 (55) & 2.2:1 \\
3 & 9 & 1.1 & B & 45 (42) & 23:1 \\
4 & 9 & 2.2 & B & 91 (89) & 10:1 \\
5 & 10 & 1.1 & A & 13 (12) & 1:1.4 \\
6 & 10 & 2.2 & A & 37 (35) & 2:1 \\
7 & 10 & 3.3 & A & 40 (39) & 1.2:1 \\
8 & 10 & 1.1 & B & 18 (17) & 2.5:1 \\
9 & 10 & 2.2 & B & 60 (60) & 9:1 \\
10 & 10 & 3.3 & B & 95 (88) & 13:1 \\
\hline
\end{tabular}
\caption{Cross-Coupling of Chlorogermanes 2 with Halides\textsuperscript{\textsuperscript{a}}}
\end{center}
\end{table}

\begin{table}[h]
\begin{center}
\begin{tabular}{|c|c|c|c|c|}
\hline
entry & germane & halide & product & yield (\%) & ratio (7b:8b) \\
\hline
1 & 9 & 1-Bromonaphthalene\textsuperscript{c} & 7a & 54 (48) & 7:2:1 \\
2 & 9 & (4)CH\textsubscript{2}OPh & 7b & 86 (85) & 9:8:1 \\
3 & 9 & (3)CF\textsubscript{3}Ph & 7c & 70 (68) & 3:1:4 \\
4 & 9 & (4)CH\textsubscript{2}OPh & 7d & 12 (10) & 3:2 \\
5 & 9 & (4)CH\textsubscript{2}OPh & 7e & 26 (21) & 9:91 \\
6 & 9 & PhCH=CHBr & 7f & 8 (5) & 1:3 \\
7 & 10 & 2-Iodo-5-Me-thiophene & 7f & 13 (6) & 2.3 \\
8 & 10 & 1-Bromonaphthalene & 7a & 24 & 1:4:1 \\
9 & 10 & 4)CH\textsubscript{2}OPh & 7b & 48 (40) & 4:1 \\
10 & 10 & (3)CF\textsubscript{3}Ph & 7c & 48 & 3:2 \\
11 & 10 & (4)CH\textsubscript{2}OPh & 7d & 3 & 1:20 \\
12 & 10 & (4)CH\textsubscript{2}OPh & 7e & 24 (24) & 1:1 \\
13 & 10 & PhCH=CHBr & 7f & 3 (3) & 1:8 \\
14 & 10 & 2-Iodo-5-Me-thiophene & 7f & 3 (3) & 1:8 \\
15 & 11 & 1-Iodonaphthalene & 7a & 99 (96) & 35:1 \\
16 & 11 & 1-Bromonaphthalene & 7a & 90 (82) & 99:1 \\
17 & 11 & (4)CH\textsubscript{2}OPh & 7b & 88 (80) & 10:1 \\
18 & 11 & (3)CF\textsubscript{3}Ph & 7c & 95 (87) & 9:1 \\
19 & 11 & (4)CH\textsubscript{2}OPh & 7d & 99 (88) & 99:1 \\
20 & 11 & (4)CH\textsubscript{2}OPh & 7e & 91 (91) & 99:1 \\
21 & 11 & PhCH=CHBr & 7f & 30 (28) & 3:1 \\
22 & 10 & 2-Iodo-5-Me-thiophene & 7f & 45 (35) & 3:2 \\
\hline
\end{tabular}
\caption{Cross-Coupling of Chlorogermanes 9–11 with Halides\textsuperscript{\textsuperscript{a}}}
\end{center}
\end{table}
with phenyl nonaflate.\textsuperscript{1,26} In addition, the fluorination of the bulky chlorogermanes may be accelerated by the addition of water as was reported for hindered chlorosilanes.\textsuperscript{27}

Mixing of 6 with TBAF in benzene-$d_6$ at ambient temperature showed the formation of a distinctive septet at $\delta -194.3$ ($\langle J_{F-H} \rangle \sim 6.0$ Hz) for PhGeMe$_2$F in agreement with the literature report for similar compounds.\textsuperscript{11} Prolonged time and/or heating promoted equilibration with perfluorinated species [$\delta -150.8$ (br s), $-126.4$ (br s)] analogous to the reported hypervalent tin\textsuperscript{28–30} and silicon\textsuperscript{31–33} species, which were successfully utilized in cross-coupling reactions.

We have demonstrated that arylchlorogermanes undergo Pd-catalyzed cross-couplings with aryl halides in the presence of TBAF in wet toluene. One chloride ligand on Ge center allows efficient activation by fluoride to promote transfer of up to three aryl groups from germane. The methodology shows that organogermanes can render a coupling efficiency comparable to the more established stannane and silane counterparts.

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**Supporting Information Available:** General experimental details and GC/MS and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.


