doi:10.1246/cl.2011.967
Published on the web September 5, 2011

Chemoselective Transfer of Allyl or Phenyl Group from Allyl(phenyl)germanes in Pd-catalyzed Reactions with Aryl Halides

Jean-Philippe Pitteloud, Yong Liang, and Stanislaw F. Wnuk*
Department of Chemistry and Biochemistry, Florida International University, Miami, Florida 33199, USA

(Received May 27, 2011; CL-110451; E-mail: wnuk@fiu.edu)

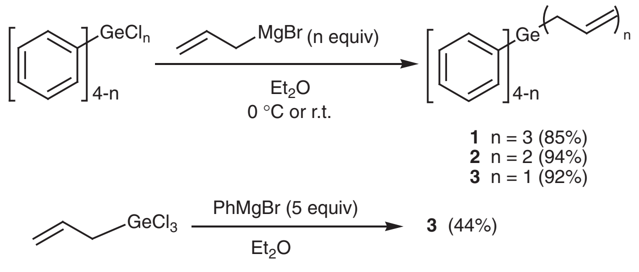
Treatment of chloro(phenyl)germanes with allylmagnesium bromide yielded allyl(phenyl)germanes. Coupling of the allyl(phenyl)germanes with aryl halides in 1,4-dioxane in the presence of aqueous NaOH and Pd catalyst resulted in Heck-type transfer of the allyl group providing the corresponding allylated aryls. On the other hand, reaction of allyl(phenyl)germanes with SbF_5 intercalated in graphite in toluene and subsequent treatment of the resulting germanyl fluorides with TBAF generates reactive hypervalent fluorogermanates that undergo Stille-like Pd-catalyzed cross-coupling with aryl halides in wet toluene to provide biaryls.

The application of organogermanes to Pd-catalyzed couplings has thus far received much less attention[1] than the couplings involving organostannanes and organosilanes.[2] 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.[3]

Based on the available knowledge on the susceptibility of organogermanes toward coupling, it appears that the coupling is promoted either by: (*i*) intramolecular chelation of a pendant Lewis basic heteroatom which renders the Ge center "permanently" pentavalent[4–7] or (*ii*) the presence of at least one heteroatom bound to the Ge center that renders the Ge center more susceptible to coordination by an external Lewis basic ligand (e.g., fluoride, hydroxide, etc.), thereby also rendering the Ge center pentavalent.[8–17] Although the effects of fluoride/base activation and Pd-catalyst/ligand combination on the coupling of organogermanes are still ambiguous, all but one[4] successful example of germane couplings with aryl/alkenyl halides involved activation with either base or fluoride.

Recently we reported that trichloro(phenyl)-, dichloro(diphenyl)-, and chloro(triphenyl)germanes undergo Pd-catalyzed cross-couplings with aryl bromides and iodides in the presence of TBAF in toluene with addition of a *measured* amount of water. One chloride ligand on the Ge center is sufficient to allow efficient activation by fluoride and subsequent transfer of one, two or three phenyl groups from the organogermane precursors.[16,17] We showed that arylchlorogermanes can render a coupling efficiency *comparable* to that of the more established stannane and silane counterparts and that their coupling efficiency reflected their ability to generate reactive hypervalent intermediates upon fluoride activation.[17]

Hiyama and co-workers utilized tri-, di-, and monoallyl(aryl)silanes in Pd-coupling with aryl halides to access biaryls.[18] They suggested that allylsilanes spontaneously cleave upon treatment with TBAF and an appropriate amount of water to provide an active silicate species that promotes transmetalation. Although the chemistry of allylgermanes is well established,[19,20] the application of allyl organogermanes as substrates for the Pd-catalyzed cross-coupling with aryl halides has not been investigated. Herein, we report chemoselective application of tri-, di-, and monoallyl(phenyl)germanes toward Pd-catalyzed reactions.



Scheme 1. Synthesis of allyl(phenyl)germanes **1**–**3**.

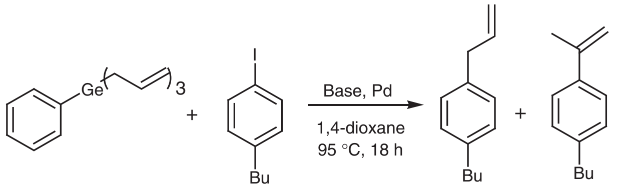
Treatment of $PhGeCl_3$, Ph_2GeCl_2, or Ph_3GeCl with 3, 2, or 1 equiv of allylmagnesium bromide yielded stable triallyl(phenyl)germane (**1**), diallyl(diphenyl)germane (**2**), or allyl(triphenyl)germane (**3**), respectively (Scheme 1). Moreover, treatment of allyl(trichloro)germane with phenylmagnesium bromide also produced allyl(triphenyl)germane (**3**) (44%).[21]

Attempted coupling of triallyl(phenyl)germane (**1**) with aryl iodides employing conditions used for the reactions of triallyl(phenyl)silanes[18] ($PdCl_2$/TBAF/PCy_3/DMSO/H_2O) or vinyltris(trimethylsilyl)germanes[12] (NaOH/H_2O/H_2O_2/[$Pd(PPh_3)_4$]/THF) with ArX failed to yield biaryl products and resulted in the recovery of **1**. However, treatment of **1** with 1-butyl-4-iodobenzene (**4a**) (18 h, 95 °C), under conditions employed for the coupling of trichloro(phenyl)germanes[9] [NaOH (8 equiv)/H_2O/dioxane/$Pd(OAc)_2$], yielded 1-allyl-4-butylbenzene (**5a**) resulting from the transfer of the allyl group (Table 1, Entry 1). The α-methyl vinyl isomer **6a** was also formed (**5a**/**6a**; 55% total, 87:13). These unexpected findings prompted us to examine the effect of reaction parameters on the transfer of allyl group from germane precursors **1**–**3**.

Thus, treatment of **1** with **4a** at higher concentrations of NaOH afforded a regioisomeric mixture of **5a** and **6a** in higher yields (Entries 2 and 3). The combination of NaOH and Pd catalyst proved to be critical for the transfer of allyl groups from **1**, since reactions with only $Pd(OAc)_2$ yielded product **5a** in much lower yield (Entry 4). The use of different Pd catalysts also gave coupling products with similar yields and regioselectivity (Entries 5 and 6). Reactions employing Et_3N and TBAF afforded **5a** in moderate yields (Entries 7 and 8). The ratio of isomers **5a**/**6a** seems to be independent of the reaction conditions. For example, temperature has no effect on regioselectivity of the reaction of allylgermane **1** with **4a**. Thus, increasing the temperature from 50 to 70 to 95 °C increased the reaction rate but the same ratio of the isomeric products **5a**/**6a** ($\approx$90:10) was observed after 1 h at all temperatures and remained constant after prolonged heating.

To further investigate the transfer of the allyl group, the reactions of allylgermanes **1**, **2**, or **3** with other aryl iodides **4a**–**4c** (1.05 equiv) were carried out (Table 2). We found that triallylgermane **1** gave higher yields of allylated aryl products **5a**–**5c** than diallylgermane **2**, which in turn were more efficient than

Table 1. Effect of the various reaction parameters on the efficiency of transferring allyl group from triallyl(phenyl)germane (**1**)[a]



1 **4a** **5a** **6a**

Entry	Base	Base /equiv	Pd	Yield /%[b,c]	Ratio[c] **5a**:**6a**
1	NaOH	8	$Pd(OAc)_2$	55	87:13
2	NaOH	10	$Pd(OAc)_2$	60	89:11
3	NaOH	12	$Pd(OAc)_2$	84	82:18
4	NaOH	—	$Pd(OAc)_2$	15	94:6
5	NaOH	12	$Pd(PPh_3)_4$	78	84:16
6	NaOH	12	$Pd_2(dba)_3$	85	86:14
7	Et_3N	10	$Pd(OAc)_2$	32	83:17
8	TBAF	10	$Pd(PPh_3)_4$	42	82:18

[a] Couplings were performed on 0.16 mmol scale of **1** (0.03 M) with 1.05 equiv of **4a** and 0.08 equiv of Pd catalyst in dioxane (5 mL) and a given stoichiometric amount of NaOH (2 M) or other bases. [b] Overall yield of **5a** and **6a**. [c] Determined by GC-MS of the crude reaction mixture.

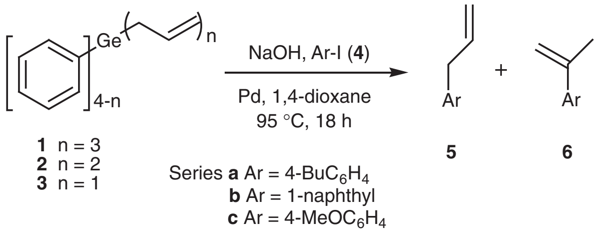
allylgermane **3** in transferring allyl groups (e.g., Entries 1–3). The use of $Pd_2(dba)_3$ afforded the products **5a**–**5c** in slightly higher yields, though the **5** to **6** regioselectivity was not improved (e.g., Entries 1–3 vs. 4–6). The bulkier 1-iodonaphthalene (**4b**) showed a small enhancement in the regioselectivity as compared to **4a** (e.g., Entry 1 vs. 7). Transfer of the allyl group from allylgermanes also occurred efficiently with p-$MeOC_6H_4I$ (**4c**) (Entries 13–15) but failed with p-$CF_3C_6H_4I$.

Since triallylgermane **1** could transfer up to three allyl substituents in the reaction with aryl halides, experiments with 3 equiv of 1-iodonaphthalene (**4b**) were attempted. Thus, treatment of **1** with **4b** under the optimized conditions [NaOH (12 equiv)] gave a mixture of **5b**/**6b** (92%, 87:13, Scheme 2). Couplings of diallylgermane **2** or allylgermane **3** with 3 equiv of **4b** provided isomers **5b**/**6b** in 78% and 38%, respectively, in addition to unchanged **4b**. It is noteworthy that coupling yields increased proportionally with the number of allyl groups present at the Ge center (38% → 78% → 92%) while the isomeric ratios **5b**/**6b** remained similar. Since the overall yield for the couplings with allylgermanes **1** and **2** never *exceeded* 100% (based on germanes as limiting reagents), it seems likely that only one allyl group from the germane substrates participated in the couplings.

It seems feasible that the formation of products **5** and **6** from allyl(phenyl)germanes **1**–**3** in the presence of NaOH might follow a Heck coupling mechanism. Allylgermatranes[5] and allyltrimethylsilanes[22] were reported to undergo Heck reaction with aryl halides via the initial addition of the aryl–Pd complex to a double bond of the allyl group. Addition of the aryl group to a less hindered γ-carbon of the allyl substituent on germanes could account for the observed regioselectivity. Coupling of vinyltributylgermanes with aryl halides has recently been shown to occur more efficiently under Heck than Stille conditions.[7]

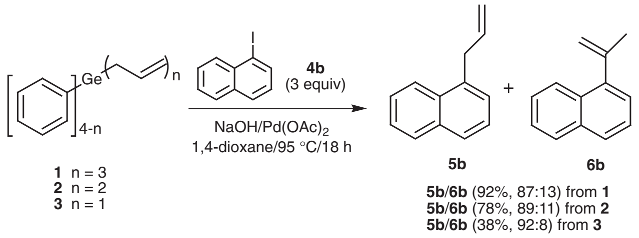
In our search to find suitable conditions for the cleavage of Ge–allyl bond and to generate reactive germanate species for subsequent transmetalation, we found that treatment of allyl(phenyl)germanes **3** or **2** with SbF_5 (0.25–0.5 equiv) intercalated in graphite[23] in toluene (0.5–1 h, 50 °C) resulted in disappearance of the germane substrates (TLC, ^1H NMR) and *clean* formation[24,25] of the fluorogermanes Ph_3GeF (s, δ −202.3, ^{19}F NMR) or Ph_2GeF_2 (2 × s, δ −165.2, and −167.4), respectively, with spectroscopic data in agreement with the reported values.[15,17] Analogous treatment of **1** gave cluster of peaks at δ −140.2 to −159.7. Treatment of the fluorogermane generated in situ from **2**/SbF_5 with **4b** in TBAF/toluene resulted in transfer of phenyl groups from Ge producing biaryl **7b** in addition to the homocoupling by-product **8b** with no formation of the allylated product **5b** (or **6b**) (Table 3). We found that addition of at least 3 equiv of TBAF was required to produce **7b** in maximum yield (Entries 1–5). Apparently, selective cleavage of the Ge–allyl bond with SbF_5 and subsequent treatment of the resulting germanyl fluorides with TBAF generates reactive hypervalent fluorogermanates that pro-

Table 2. Allylation of aryl iodides with allyl(phenyl)germanes **1**–**3**[a]



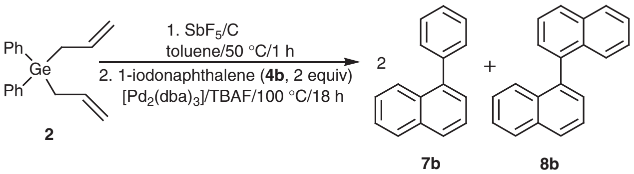
Entry	Germane	Ar–I	Pd	Yield /%[b,c]	Ratio[c] **5**:**6**
1	**1**	**4a**	$Pd(OAc)_2$	78	82:18
2	**2**	**4a**	$Pd(OAc)_2$	47	82:18
3	**3**	**4a**	$Pd(OAc)_2$	32	86:14
4	**1**	**4a**	$Pd_2(dba)_3$	80	86:14
5	**2**	**4a**	$Pd_2(dba)_3$	55	85:15
6	**3**	**4a**	$Pd_2(dba)_3$	33	85:15
7	**1**	**4b**	$Pd(OAc)_2$	73	90:10
8	**2**	**4b**	$Pd(OAc)_2$	51	90:10
9	**3**	**4b**	$Pd(OAc)_2$	29	91:9
10	**1**	**4b**	$Pd_2(dba)_3$	88	91:9
11	**2**	**4b**	$Pd_2(dba)_3$	69	92:8
12	**3**	**4b**	$Pd_2(dba)_3$	40	93:7
13	**1**	**4c**	$Pd(OAc)_2$[d]	90	79:21
14	**2**	**4c**	$Pd(OAc)_2$[e]	37	76:24
15	**3**	**4c**	$Pd(OAc)_2$[f]	15	73:27

[a] Couplings were performed on 0.16 mmol scale of germanes **1**–**3** (0.03 M) with 1.05 equiv of aryl halides, 12 equiv of NaOH, and 0.08 equiv of Pd catalyst. [b] Overall yield of **5a** and **6a**. [c] Based on GC-MS and ^1H NMR of the purified reaction mixture. [d] With [$Pd_2(dba)_3$] (56%, 81:19). [e] With [$Pd_2(dba)_3$] (39%, 79:21). [f] With [$Pd_2(dba)_3$] (14%, 80:20).



Scheme 2. Coupling of allyl(phenyl)germanes **1**–**3** with excess of 1-iodonaphthalene (**4b**).

Table 3. SbF_5-promoted coupling of diallyl(diphenyl)germane (**2**) with 1-iodonaphthalene (**4b**): Transfer of the phenyl groups from Ge[a]



2 **7b** **8b**

Entry	Germane	TBAF[b] /equiv	Yield **7b**/%[c,d]	Ratio[d] **7b**:**8b**
1	**2**	1	43	4.4:1
2	**2**	2	53	3.9:1
3	**2**	3	60 (54)	3.8:1
4	**2**	4	47	2.0:1
5	**2**	5	44	1.3:1
6	**2**	3[e]	67 (59)	5.2:1
7	**2**	3[f]	72 (62)	5.6:1
8	**2**	3[g]	68	6.1:1

[a]Couplings were performed on 0.14 mmol scale of germanes **2** (0.04 M) with 2 eqiuv of **4b** and 0.05 equiv of Pd catalyst. [b]Commercial 1 M THF solution containing 5% H_2O. [c]Based upon transferring of two phenyl groups from **2**. Isolated yield in parenthesis. [d]Based on GC-MS of the crude reaction mixture. [e]With 25 µL of H_2O added. [f]With 50 µL H_2O. [g]With 75 µL H_2O.

mote transmetalation via a Stille-like mechanism. Treatment of **2** with SbF_5/C alone, as a fluoride source, failed to produce cross-coupling product **7b**. The yield increased when couplings were performed with addition of a *measured* amount of water (≈10–30 equiv; Entries 6–8), as observed before for couplings with chloro(phenyl)germanes.[16,17] The SbF_5/TBAF combination in moist toluene allowed transfer of two phenyl groups from germane **2**, as expected based on the couplings of Ph_2GeCl_2 with aryl halides promoted by TBAF.[17]

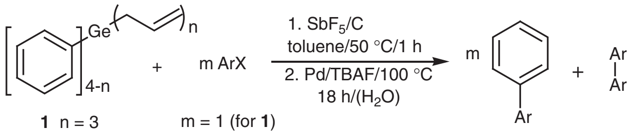
One-pot treatment of germanes **1**, **2**, or **3** with SbF_5/C followed by Pd-catalyzed (TBAF/moist toluene) reactions with 1, 2, or 3 equiv of aryl halides, respectively afforded various biaryls **7b**–**7d** in good yields and regioselectivity (Table 4). Couplings with 1-bromonaphthalene also afforded **7b** although in lower yields than with iodonaphthalene.

In summary, we have developed two chemoselective Pd-catalyzed reactions with allyl(phenyl)germanes. One reaction allows for the selective transfer of the allyl group in the reaction with aryl halides mediated by NaOH providing allylaryls, while the second reaction allows for the selective transfer of the phenyl group from Ge center yielding biaryls upon treatment with SbF_5/C and TBAF.

This work was supported by an award from NIH/NCI (5SC1CA138176) and FIU University Graduate School Dissertation Year Fellowship to JPP.

This paper is in celebration of the 2010 Nobel Prize awarded to Professors Richard F. Heck, Akira Suzuki, and Ei-ichi Negishi.

Table 4. SbF_5-promoted coupling of germanes **1**–**3** with aryl halides[a]



1 n = 3
2 n = 2
3 n = 1

m = 1 (for **1**)
m = 2 (for **2**)
m = 3 (for **3**)

7b-d **8b-d**

Entry	Germane	Ar–X	Product	Yield **7**/%[b,c]	Ratio[c] **7**:**8**
1	**1**	1-Iodonaphthalene	**7b**	52 (45)	10:1
2	**1**	1-Bromonaphthalene	**7b**	42	15:1
3	**1**	$4\text{-}CH_3OC_6H_4I$	**7c**	82 (71)	20:1
4	**1**	$4\text{-}CF_3C_6H_4I$	**7d**	46 (41)	1.9:1
5	**2**	1-Iodonaphthalene	**7b**	72 (62)	5.6:1
6	**2**	1-Bromonaphthalene	**7b**	34	2.3:1
7	**2**	$4\text{-}CH_3OC_6H_4I$	**7c**	45	2.8:1
8	**2**	$4\text{-}CF_3C_6H_4I$	**7d**	33	1:1
9	**3**	1-Iodonaphthalene	**7b**	71 (63)	4:1
10	**3**	1-Bromonaphthalene	**7b**	14	3.3:1
11	**3**	$4\text{-}CH_3OC_6H_4I$	**7c**	32	1.6:1
12	**3**	$4\text{-}CF_3C_6H_4I$	**7d**	22	1:1.5

[a]Couplings were performed on 0.14 mmol scale of germanes (**1**–**3**; 0.04 M) with 0.05 equiv of $Pd_2(dba)_3$ catalyst and 1.0 (for **1**), 2.0 (for **2**), or 3.0 (for **3**) equiv of halides and TBAF/(1 M/THF, 3 equiv)/water (50 µL). [b]Based upon transferring of one, two, or three phenyl groups from **1**, **2**, or **3**, respectively. Isolated yield in parenthesis. [c]Determined by GC-MS of the crude reaction mixture.

References and Notes

1 A. C. Spivey, C. J. G. Gripton, J. P. Hannah, *Curr. Org. Synth.* **2004**, *1*, 211.
2 *Metal-Catalyzed Cross-Coupling Reactions*, ed. by A. de Meijere, F. Diederich, Wiley-VCH, Weinheim, Germany, **2004**.
3 *The Chemistry of Organic Germanium, Tin and Lead Compounds*, ed. by S. Patai, John Wiley & Sons, Chichester, **1995**, Vol. 1; *The Chemistry of Organic Germanium, Tin and Lead Compounds*, ed. by Z. Rappoport, John Wiley & Sons, Chichester, **2002**, Vol. 2.
4 M. Kosugi, T. Tanji, Y. Tanaka, A. Yoshida, K. Fugami, M. Kameyama, T. Migita, *J. Organomet. Chem.* **1996**, *508*, 255.
5 J. W. Faller, R. G. Kultyshev, *Organometallics* **2002**, *21*, 5911.
6 J. W. Faller, R. G. Kultyshev, J. Parr, *Tetrahedron Lett.* **2003**, *44*, 451.
7 N. M. Torres, J. M. Lavis, R. E. Maleczka, Jr., *Tetrahedron Lett.* **2009**, *50*, 4407.
8 T. Nakamura, H. Kinoshita, H. Shinokubo, K. Oshima, *Org. Lett.* **2002**, *4*, 3165.
9 T. Enokido, K. Fugami, M. Endo, M. Kameyama, M. Kosugi, *Adv. Synth. Catal.* **2004**, *346*, 1685.
10 M. Endo, K. Fugami, T. Enokido, H. Sano, M. Kosugi, *Adv. Synth. Catal.* **2007**, *349*, 1025.
11 S. F. Wnuk, P. I. Garcia, Jr., Z. Wang, *Org. Lett.* **2004**, *6*, 2047.
12 Z. Wang, S. F. Wnuk, *J. Org. Chem.* **2005**, *70*, 3281.
13 Z. Wang, A. Gonzalez, S. F. Wnuk, *Tetrahedron Lett.* **2005**, *46*, 5313.
14 A. C. Spivey, C.-C. Tseng, J. P. Hannah, C. J. G. Gripton, P. de Fraine, N. J. Parr, J. J. Scicinski, *Chem. Commun.* **2007**, 2926.
15 A. C. Spivey, C. J. G. Gripton, J. P. Hannah, C.-C. Tseng, P. de Fraine, N. J. Parr, J. J. Scicinski, *Appl. Organomet. Chem.* **2007**, *21*, 572.
16 Z.-T. Zhang, J.-P. Pitteloud, L. Cabrera, Y. Liang, M. Toribio, S. F. Wnuk, *Org. Lett.* **2010**, *12*, 816.
17 J.-P. Pitteloud, Z.-T. Zhang, Y. Liang, L. Cabrera, S. F. Wnuk, *J. Org. Chem.* **2010**, *75*, 8199.
18 A. K. Sahoo, T. Oda, Y. Nakao, T. Hiyama, *Adv. Synth. Catal.* **2004**, *346*, 1715.
19 A. C. Spivey, C. M. Diaper, *Sci. Synth.* **2003**, *5*, 181.
20 T. Akiyama, in *Main Group Metals in Organic Synthesis*, ed. by H. Yamamoto, K. Oshima, Wiley-VCH, Weinheim, **2004**, Vol. 2, pp. 593–619.
21 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.
22 K. Karabelas, C. Westerlund, A. Hallberg, *J. Org. Chem.* **1985**, *50*, 3896.
23 R. J. P. Corriu, J. M. Fernandez, C. Guerin, *J. Organomet. Chem.* **1980**, *192*, 347.
24 Activated C(sp^3)–Ge bonds in allylgermanes can be cleaved in the presence of Lewis acids.[20,23]
25 Treatment of **1**[15] or **2** with TBAF did not affect cleavage of Ge–allyl bond(s) since formation of fluorogermane(s) was not observed on ^1H or ^{19}F NMRs.