

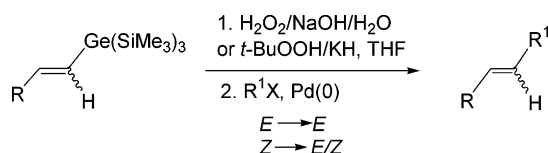
Application of Vinyl Tris(trimethylsilyl)germanes in Pd-Catalyzed Couplings

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R = alkyl or aryl, R¹ = aryl, alkenyl; X = I, Br, Cl or OTf

The oxidative treatment of vinyltris(trimethylsilyl)germanes with hydrogen peroxide (NaOH/H₂O/THF) or *tert*-butyl peroxide (KH/THF) generates reactive germanol or germanoxane species that undergo Pd-catalyzed cross-couplings with aryl and alkenyl halides and aryl triflates in the presence of Pd(PPh₃)₄. Vinylgermanes having either a conjugated or isolated double bond serve as versatile transmetalation reagents. The *E*-germanes undergo coupling with retention of stereochemistry under aqueous and anhydrous conditions, while coupling of *Z*-germanes occurs with less stereoselectivity to produce a mixture of *E/Z* products.

Despite the wide application of organostannanes (Stille)¹ and organosilanes (Hiyama)² to coupling reactions, the Pd-catalyzed coupling of organogermanes has received little attention,^{3,4} although germanium is located between silicon and tin in the periodic table. The development of organogermanes as transmetalation reagents in Pd-catalyzed cross-coupling reactions has been limited by the lower reactivity of tetracoordinated organogermanium species³ and the complexity of syntheses of vin-

ylgermanyl derivatives.⁵ In fact, the lower reactivity of vinyl trialkyl- and triarylgermanes, as compared to the corresponding silanes,^{6a} stannanes,^{6b} and halides,^{6c} has been employed to advantage in organic synthesis. For example, doubly substituted α -germanyl- β -stannyl(or silyl or halo)alkenes undergo Pd-catalyzed couplings chemoselectively at the β carbon to afford α -germanyl- β -substituted alkenes.⁶

The first example of a Pd-catalyzed coupling involving organogermanes was the reaction of styryltrimethylgermanes with aryl tetrafluoroborate.^{3a} Kosugi et al. later reported that 1-aza-5-germa-5-organobicyclo[3,3,1]undecanes (carbagermatranes) are much more reactive than tetracoordinated germanes in the cross-coupling reactions with aryl bromides owing to the internal coordination of nitrogen to germanium.^{3b} Faller and Kultyshev found that allyl-, aryl-, alkenyl-, and alkynylloxagermatranes undergo coupling with aryl iodides.^{3c} They also demonstrated that organogermatranes are more efficient than triethoxygermanes and that coupling is promoted by fluoride (as in a case of coupling of organosilanes²). Oshima and co-workers showed that aryltri(2-furyl)germanes are viable reagents for biaryl synthesis.^{3d} We recently communicated that vinyl tris(trimethylsilyl)germanes can be employed in Pd-catalyzed cross-coupling reactions with aryl halides.⁴ Herein, we report application of various tris(trimethylsilyl)germanes as transmetalation reagents in cross-coupling reactions with aryl halides and triflates as well as alkenyl bromides under oxidative conditions in either aqueous or anhydrous conditions.

The *E*-vinyltris(trimethylsilyl)germane (TTMS-germane) precursors **2a,b** were conveniently prepared (51–81%) by stereoselective radical-mediated germlydesulfonations of the *E*-vinyl sulfones **1** with (Me₃Si)₃GeH (Scheme 1).^{4,7} The *Z*-germanes **4a,c–f** were synthesized (80–98%) by radical hydrogermylation of the corresponding alkynes **3** with (Me₃Si)₃GeH.⁸

We found that vinyl TTMS-germanes **2** and **4** under oxidative conditions can serve as good nucleophiles in coupling reactions. Thus, treatment of the conjugated germane **2a(E)** with H₂O₂ in the presence of NaOH in aqueous THF (method A) followed by addition of iodobenzene and Pd(PPh₃)₄ gave *E* stilbene **5a** (50%, Table 1, entry 1). Coupling of **2a(E)** with bromobenzene afforded **5a(E)** in 88% yield (entry 2). The reaction seems

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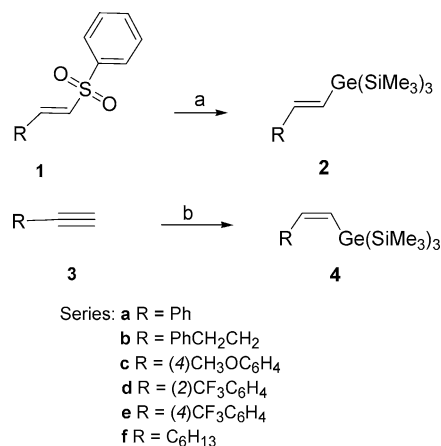
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(7) Attempted catalytic (H₂PtCl₆) hydrogermylation of phenylacetylene **3a** with (Me₃Si)₃GeH produced **4a(Z)** predominantly, as opposed to the hydrosilylation with chlorodi(isopropyl)silane^{2c} which afforded the corresponding *E*-alkene.

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SCHEME 1. Stereoselective Synthesis of *E*- (2) and *Z*-Vinyl Tris(trimethylsilyl)Germanes (4)^a

^a Reagents and conditions: (a) (Me₃Si)₃GeH/AIBN/toluene or benzene (80 °C; oil bath); (b) (Me₃Si)₃GeH/AIBN/benzene (25 °C or Δ).

TABLE 1. Pd-Catalyzed Coupling of the *E*-Vinyl TTMS-germanes 2 (See Scheme 1 for Description of R in Substrates 2)

		H ₂ O ₂ /NaOH/H ₂ O (Method A) or <i>t</i> -BuOOH/KH (Method B)					
		R ¹ X, (Ph ₃ P) ₄ Pd					
		THF/45°C/10 h					
						5 R ¹ = Ph	
entry	substrate	R ¹	X	product ^a	yield ^{b,c} A (%)	yield ^{c,d} B (%)	
1	2a	Ph	I	5a	50	80	
2	2a	Ph	Br	5a	88	50	
3	2a	Ph	Cl	5a	37 ^e	10 ^f	
4	2a	Ph	OTf	5a	15 ^e	20 ^f	
5	2b	Ph	I	5b	51	80	
6	2b	Ph	Br	5b	73	<5	

^a *E* isomer only (based on ¹H NMR or GC–MS). ^b Isolated yield (method A). ^c Average yield from two independent experiments. ^d Isolated yield (method B). ^e *E*/*E* isomer of 1,4-diphenyl-1,3-butadiene was also isolated. ^f *E*/*E* and *E*/*Z* isomers of 1,4-diphenyl-1,3-butadiene were also isolated.

to be general in character, and even less reactive⁹ chlorobenzene (entry 3) and phenyl triflate (entry 4) yielded 5a(*E*) stereoselectively, though in lower yields. Also, the nonconjugated vinyl germane 2b(*E*) underwent coupling with iodo- and bromobenzene to give 1,4-diphenyl-1-butene 5b(*E*) (51% and 73%, entries 5 and 6).

The *E*-germanes 2 also underwent coupling under anhydrous conditions. Thus, treatment of 2a(*E*) with *tert*-butyl peroxide in the presence of KH in THF¹⁰ (method B) followed by reactions with aryl halides or triflate gave coupled product 5a (method B; entries 1–4). The non-

TABLE 2. Pd-Catalyzed Coupling of the *Z*-Vinyl TTMS-germanes 4 (See Scheme 1 for Description of R in Substrates 4)

		H ₂ O ₂ /NaOH/H ₂ O (Method A) or <i>t</i> -BuOOH/KH (Method B)				
4		R ¹	R ¹ X, (Ph ₃ P) ₄ Pd THF/45°C/10 h	5 R ¹ = Ph 6 R ¹ = CH=CHPh		
entry	sub- strate	R ¹	X	product	yield ^{a,b} A (<i>E/Z</i>) ^{b,c}	yield ^{b,d} B (<i>E/Z</i>) ^{b,c}
1	4a	Ph	I	5a	60 (33/67)	83 (3/97)
2	4a	Ph	Br	5a	53 (50/50)	78 (8/92)
3	4a	Ph	Cl	5a	44 (67/33) ^e	<5
4	4a	Ph	OTf	5a	33 (98/2) ^e	<5
5	4c	Ph	I	5c	90 (13/87)	96 (3/97)
6	4c	Ph	Br	5c	50 (64/36)	10 (2/98) ^f
7	4c	PhCH=CH	Br ^g	6c	66 ^{e,f,h}	52 ^{e,f,i}
8	4d	Ph	I	5d	41 (21/79)	77 (1/99)
9	4d	Ph	Br	5d	30 (76/24)	15 (3/97) ^j
10	4e	Ph	I	5e	80 (55/45)	71 (5/95)
11	4e	Ph	Br	5e	68 (99/1)	58 (1/99)
12	4e	Ph	Cl	5e	15 (56/44) ^k	<5
13	4f	Ph	I	5f	36 (45/55)	60 (25/75)
14	4f	Ph	Br	5f	64 (33/67)	60 (20/80)
15	4f	PhCH=CH	Br ^g	6f	67 ^{e,l}	<5

^a Isolated yield (method A). ^b Based on two independent experiments. ^c Based on ¹H NMR and/or GC–MS. ^d Isolated yield (method B). ^e *E*/*E* isomer of 1,4-diphenyl-1,3-butadiene was also isolated. ^f Isomers of 1,4-di(4-methoxyphenyl)-1,3-butadiene were also isolated (2–30%). ^g *E*/*Z* mixture (~88:12) of *β*-bromostyrene was used. ^h 1*E*,3*E*/1*Z*,3*E* (27:73). ⁱ 1*E*,3*E*/1*Z*,3*E* (18:82). ^j Isomers of 1,4-di(2-trifluoromethylphenyl)-1,3-butadiene were also isolated (20%). ^k Isomers of 1,4-di(4-trifluoromethylphenyl)-1,3-butadiene were also isolated. ^l 1*E*,3*E*/1*E*,3*Z* (34:66).

conjugated 2b(*E*) underwent coupling with iodobenzene (entry 5). The couplings in anhydrous conditions occurred again with retention of *E* stereochemistry and with yields as high as 80% for the reactions with iodobenzene (entries 1 and 5). Interestingly, coupling yields were higher for bromobenzene in aqueous conditions while iodobenzene gives better yields under anhydrous conditions.

The (*Z*) TTMS-germanes 4a,c–e were equally reactive. Thus, coupling of 4a,c–e(*Z*) with aryl iodides and bromides under aqueous conditions (H₂O₂/NaOH) gave stilbenes 5a,c–e (30–90%, Table 2). Again, reactions with chlorobenzene and phenyl triflate occurred in lower yields (15–44%, entries 3, 4 and 12). The coupling of 4a,c–e with aryl halides and triflate led to the formation of *E*/*Z* stilbenes 5a,c–e. Yields and retention of *Z* stereochemistry were higher for iodobenzene than for bromobenzene and decrease further for chlorobenzene and triflate (for example, entries 1–4). In fact, the least reactive phenyl triflate coupled with 4a(*Z*) to give predominantly *E*-stilbene 5a (*E*/*Z*, 98:2; entry 4).

The substituents on the phenyl ring, e.g., 4a vs 4c–e (*p*-MeO, *p*-CF₃, or *o*-CF₃) did not have a significant effect on yield and stereochemistry (entries 5, 6, and 8–12). The aliphatic germane 4f(*Z*) coupled with iodo- and bromobenzenes to give *E*/*Z* mixtures of 1-phenyl-1-decene 5f (entries 13 and 14).

Not only aryl halides but also vinyl halides can be employed. Thus, oxidative treatment (method A) of 4c(*Z*)-with 1.5 equiv of *β*-bromostyrene gave 1-(4-methoxyphenyl)-4-phenyl-1,3-butadiene 6c (66%, entry 7). Coupling of 4f(*Z*) with *β*-bromostyrene (*E*/*Z*, ~88:12) gave

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6f (67%, entry 15). The aliphatic vinyl bromides [e.g., 2-bromo-2-butene (*E/Z*, ~1:1) and 1-bromo-2-methyl-1-propene] failed to couple with organogermanes **4a** and **4e**.

The *Z*-germanes **4a,c–f** also underwent coupling with aryl iodides and bromides as well as with β -bromostyrene under anhydrous conditions. In general, couplings under anhydrous conditions (method B) give comparable or higher yields for iodobenzene (entries 1, 5, 8, and 10) than for the bromobenzene (entries 2, 6, 9, and 11). It is noteworthy that couplings with the conjugated *Z*-germanes **4a,c–e** under anhydrous conditions occurred predominantly with the retention of *Z*-stereochemistry (*E/Z* from 8:92 to 1/99).

The two coupling procedures [aqueous (**A**) and anhydrous (**B**)] seem to complement each other with method B giving better yields and higher retention of stereochemistry for the coupling of *Z*-germanes. Interestingly, coupling of **4e(Z)** with bromobenzene gave almost complete conversion of stereochemistry under aqueous oxidative conditions while the retention of stereochemistry was observed under anhydrous conditions (entry 11).

It appears that hydrogen peroxide or *tert*-butyl peroxide cleaves the Ge–Si bond(s) in **2** and **4** [$R'Ge(SiMe_3)_3$] to generate active germanol or germanoxane species¹¹ of the type $R'Ge(OH)_n(SiMe_3)_{3-n}$ or $R'Ge(OSiMe_3)_n(SiMe_3)_{3-n}$ ($n = 1, 2$, or 3). Apparently, cleavage of group 14 element (Si)–group 14 element (Ge) σ bonds, which are known to have low oxidation potentials,¹² takes place chemoselectively and C–Ge bond is not effected by such oxidation conditions. It is noteworthy that the oxidative conditions employed for the generation of active organogermanium species are similar to the ones used in Tamao–Kumada and Fleming oxidation of silanes to alcohols that involve cleavage of C–Si bond.¹³

The major byproduct(s) isolated from the cross-coupling reactions with TTMS-germanes resulted from the oxidative homocoupling of TTMS-germanes. For example, cross-coupling between **2a(E)** and less reactive chlorobenzene or aryl triflate produced, in addition to **5a**, substantial amounts of the homocoupled byproduct, 1,4-diphenyl-1,3-butadiene [(*E,E*-isomer, method A; 23–34%) or (*E,E/E,Z*-mixture, method B; 29–36%), e.g., 46–72% consumption of **2a(E)**]. Such self-coupling of the transmetalation components (organostannanes,^{14a} silanes,^{14b–d} and boronic acids^{14e}) in Pd-catalyzed cross-couplings is known. Reductive homocoupling of halides components has been observed with β -bromostyrene (9–20% of 1,4-diphenyl-1,3-butadiene; entries 7 and 15) but generally

not with aryl halides.^{15a,b} The procedures reported herein provide examples of “ligand-free”^{15c,d} Pd-catalyzed coupling of organogermanes with aryl and alkenyl halides. It is also noteworthy that no activation with fluoride was necessary and reaction conditions were usually milder than those reported previously.³

In summary, we have demonstrated that conjugated and nonconjugated vinyl tris(trimethylsilyl)germanes successfully undergo Pd-catalyzed cross-couplings with aryl and alkenyl halides and aryl triflates under aqueous and anhydrous oxidative conditions. In contrast to *E*-germanes, which undergo coupling with retention of stereochemistry under both conditions, coupling of *Z*-germanes occurred with less stereoselectivity to produce *E/Z* mixture of products with anhydrous conditions being more stereoselective.

Experimental Section

Detailed experimental procedures are described in Supporting Information. Vinyl sulfones **1a** and **1b** were prepared as reported.⁴ Acetylenes **3a** and **3c–f** were commercially available.

(*E*)-2-Phenyl-1-[tris(trimethylsilyl)germyl]ethene (**2a**).

Procedure A. Argon was bubbled through a solution of **1a(E)** (450 mg, 1.84 mmol) in anhydrous benzene or toluene (25 mL) for 15 min. $(Me_3Si)_3GeH$ (0.97 mL, 902 mg, 3 mmol) and AIBN (308 mg, 1.84 mmol) were added, and degassing of oxygen was continued for 10 min more and then the solution was heated at 80 °C (oil bath) for 6 h. The volatiles were evaporated, and the oily residue was column chromatographed (hexane) to give **2a**⁴ (590 mg, 81%): IR (neat) 2952, 1598, 1397, 1246 cm^{-1} ; ¹H NMR δ 0.30 (s, 27H), 6.72 (d, $J = 18.5$ Hz, 1H), 6.86 (d, $J = 18.5$ Hz, 1H), 7.23 (t, $J = 7.1$ Hz, 1H), 7.34 (t, $J = 7.5$ Hz, 2H), 7.39 (d, $J = 7.0$ Hz, 2H); ¹³C NMR δ 2.0, 126.2, 126.4, 127.4 (C1), 128.9, 139.6, 144.9 (C2). GC-MS (t_R 19.99 min) m/z 396 (3.5, M^+ , ⁷⁴Ge), 394 (2.0, M^+ , ⁷²Ge), 392 (1.5, M^+ , ⁷⁰Ge). Anal. Calcd for $C_{17}H_{34}GeSi_3$ (395.32): C, 51.65; H, 8.67. Found: C, 51.38; H, 8.89.

(*Z*)-2-Phenyl-1-[tris(trimethylsilyl)germyl]ethene (**4a**).

Procedure B. $(Me_3Si)_3GeH$ (0.323 mL, 300 mg, 1 mmol) was added in one portion via a syringe to a stirred solution of **3a** (0.112 mL, 104 mg, 1 mmol) in dry benzene (3 mL) at ambient temperature under nitrogen atmosphere. After 3 h, the volatiles were evaporated in vacuo and the oily residue was purified by flash chromatography on silica gel (hexane) to give **4a**^{7b} (388 mg, 98%): ¹H NMR δ 0.25 (s, 27H), 6.12 (d, $J = 13.6$ Hz, 1H), 7.15–7.35 (m, 5H), 7.41 (d, $J = 13.6$ Hz, 1H).

(*E*)-1,2-Diphenylethene (5a**). Method A.** A solution of NaOH (12 mg, 0.3 mmol) and H_2O_2 (30% solution, 20 μ L, 0.20 mmol) in deionized H_2O (0.4 mL) was added to a stirred solution of **2a** (25 mg, 0.063 mmol) in THF (3 mL) at ambient temperature. After 15 min, iodobenzene (11 μ L, 20 mg, 0.095 mmol) and $Pd(PPh_3)_4$ (7 mg, 0.006 mmol) were added, and the resulting brownish mixture was heated at 45 °C (oil bath) for 10 h. The volatiles were evaporated, and the residue was partitioned ($H_2O/CHCl_3$). The organic layer was dried ($MgSO_4$), evaporated, and purified by column chromatography (hexane) to give **5a** (5.7 mg, 50%) with data identical to a commercial sample.

(15) (a) Formation of the biphenyl byproduct with a yield of less than 5% [although aryl halides were used in excess (1.5 equiv)] has been observed in few cases. For example during synthesis of **5a(E/Z)**, **5b(E)** and **5c(E/Z)** (see Supporting Information). (b) Couplings of 4-iodotoluene with phenyl germanes resulted in the formation of the homocoupling byproduct, 4,4'-dimethylbiphenyl, in varying amounts (12–60%).^{3c} (c) Although the Pd source [$Pd(Ph_3)_4$] bears the PPh_3 ligands, this report is the example^{4,15d} of coupling reaction of organogermanes in which addition of extra ligands such as $PhAr_3$,^{3b} $AsPh_3$,^{3c} (2-furyl)₃P,^{3c,d} or $But_2P(biphenyl)$ ^{3c,e} were not required. (d) Enokido, T.; Fugami, K.; Endo, M.; Kameyama, M.; Kosugi, M. *Adv. Synth. Catal.* **2004**, *346*, 1685–1688.

(11) Oshima and co-workers have speculated that nucleophilic hypervalent organogermanium species such as $[ArGe(OH)_3F]^-$, generated from aryltri(2-furyl)germanes in the presence of TBAF, undergo transmetalation from germanium to palladium.^{3d}

(12) Cleavage of Ge–Si bond under oxidative conditions via oxygen insertion has been reported: Mochida, K.; Shimizu, H.; Kugita, T.; Nanjo, M. *J. Organomet. Chem.* **2003**, *673*, 84–94.

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Method B. KH (12 mg, 0.3 mmol) and *t*-BuOOH (5.0–6.0 M solution, 37.8 μ L, 0.19 mmol) were added to a stirred solution of **2a** (25 mg, 0.063 mmol) in THF (3 mL) at ambient temperature. After 15 min, iodobenzene (11 μ L, 20 mg, 0.095 mmol) and Pd(PPh₃)₄ (7 mg, 0.006 mmol) were added, and the resulting brownish mixture was heated at 45 °C (oil bath) for 10 h. The volatiles were evaporated and the residue was partitioned (H₂O/CHCl₃). The organic layer was dried (MgSO₄), evaporated, and purified by column chromatography (hexane) to give **5a** (9.1 mg, 80%).

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Supporting Information Available: Experimental procedures, characterization data, and copies of ¹H NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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