

Palladium-catalyzed highly regio-, stereo- and chemoselective carbogermanylation of allenes: a novel method for the synthesis of 2-arylallylgermane derivatives†

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Palladium complexes effectively catalyze the three-component assembly of allenes, aryl iodides and stannylgermane in a highly regio-, stereo- and chemoselective fashion to yield (Z)-allylgermanes in good to excellent yields.

The transition-metal-catalyzed addition of an electrophile and a nucleophile to an unsaturated species is an efficient route to construct two carbon–carbon bonds for organic synthesis.¹ However, the control of both regio- and stereoselectivity in the multi-component coupling reactions remains a great challenge to organic chemists. Recent disclosures from our laboratories revealed that allenes are very useful unsaturated substrates for palladium-catalyzed three-component assembling reactions.² Other groups have also studied this type of three-component reaction of allenes^{3–5} but most of these reactions gave poor regio- and stereoselectivity of the products.^{3,4} While several types of nucleophiles^{2–5} including amines, malonates, and organometallic compounds (B–B, Sn–Sn and Si–Sn) have been used in the three-component assembling reactions of allenes, to the best of our knowledge, no example using stannylgermanes as nucleophiles has been reported.

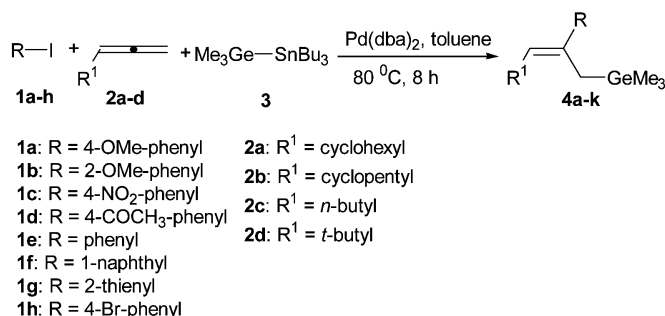
Allylgermanes are versatile organometallic reagents in organic synthesis.⁶ For example, these reagents are widely used in allylation reactions with imines⁷ and in [3 + 2] cycloaddition reactions.⁸ Although considerable attention has been paid to the synthesis of allylmetal reagents such as allylboranes, allylsilanes and allylstannanes, very few studies on the synthesis of allylgermanes have been reported.⁹ In view of the high synthetic utility and lower toxicity of allylgermanes than the corresponding organotin compounds, the development of a novel method for the synthesis is highly demanded. Our continuing interest in metal-mediated allene chemistry¹⁰ prompted us to explore the possibility of using stannylgermanes as nucleophiles in the three-component assembling reactions. In this communication, we wish to report that phosphine-free palladium complexes effectively catalyzed the three-component assembly of allenes, aryl iodides and stannylgermane leading to (Z)-allylgermanes in good to excellent yields in a highly regio-, stereo- and chemoselective fashion.

Treatment of 4-iodoanisole **1a** with cyclohexylallene **2a** and trimethyl(tributylstannyl)germane **3** in the presence of Pd(dba)₂ (5.0 mol%) in toluene at 80 °C for 8 h led to three-component assembling product **4a** in 93% yield (Scheme 1; Table 1, entry 1). No isomer other than **4a** was detected under these conditions as evidenced by the ¹H NMR spectrum of the crude reaction mixture. The catalytic reaction is completely regioselective, the aryl and the germyl group adding to the middle and terminal carbon of the allene moiety, and highly stereoselective, giving **4a** with Z-stereoselectivity greater than 99%. Control experiments verified that in the absence of a palladium catalyst, no reaction occurred.

To understand the nature of the catalytic reaction, the activities of various palladium catalysts in toluene for the

reaction of **1a** with **2a** and **3** were examined. Phosphine–palladium complexes such as PdCl₂(PPh₃)₂ and Pd(PPh₃)₄ were totally ineffective for the three-component assembling reaction. Pd(OAc)₂ and PdCl₂(PhCN)₂ were less effective, giving **4a** in 53 and 42% yields, respectively. A brief examination of the effect of solvent on the yield of **4a** using Pd(dba)₂ as the catalyst revealed that toluene was the solvent of choice. Other solvents such as THF, CH₃CN, DMF and EA (ethyl acetate) gave **4a** in 84, 82, 69 and 51% yields, respectively. The above optimization studies indicate that the selection of phosphine-free palladium complexes is crucial for the success of the three-component reaction.

The results for the three-component assembly of allenes, aryl iodides and stannylgermane catalyzed by the Pd(dba)₂–toluene system are compiled in Table 1. Several aryl iodides **1b–g** effectively undergo three-component assembling with **2a** and **3** to afford the corresponding allylgermanes **4b–g** in good to excellent yields with very high Z selectivity (entries 2–7). Electron-withdrawing substituents and electron-donating groups on the aromatic ring show little effect on the yields of the catalytic reaction (entries 1–4). The catalytic reaction is highly



Scheme 1

Table 1 Results of palladium-catalyzed three-component assembly of aryl iodides **1**, allenes **2** and stannylgermane **3**^a

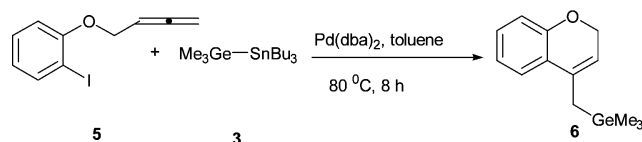
Entry	Aryl iodide	Allene	Product	Z : E ^b	Yield (%) ^c
1	1a	2a	4a	99 : 1	88 (93)
2	1b	2a	4b	99 : 1	82
3	1c	2a	4c	99 : 1	89
4	1d	2a	4d	98 : 2	90
5	1e	2a	4e	98 : 2	88
6	1f	2a	4f	98 : 2	80
7	1g	2a	4g	94 : 6	81
8	1h	2a	4h	98 : 2	83
9	1a	2b	4i	98 : 2	88
10	1a	2c	4j	94 : 6	84
11	1a	2d	4k	99 : 1	82

^a All reactions were carried out using aryl iodide **1** (1.00 mmol), allene **2** (1.50 mmol), stannylgermane **3** (1.00 mmol), Pd(dba)₂ (0.05 mmol) and toluene at 80 °C for 8 h. ^b Determined by ¹H NMR spectroscopy. ^c Isolated yields; yields in parentheses were measured from the crude products by the ¹H NMR integration method using mesitylene as an internal standard.

† Electronic supplementary information (ESI) available: synthesis and characterization of compounds **4** and **6**. See <http://www.rsc.org/suppdata/cc/b3/b305370a/>

chemoselective as evidenced by the selective reaction of 4-bromoiodobenzene **1h** with **2a** and **3** to afford 2-(4-bromophenyl)allylgermane **4h** in 83% yield (entry 8). The present arylgermylation of allenes tolerates a variety of functional groups such as methoxy, nitro, acetyl, sulfur and bromo on the aromatic ring of the aryl iodide. In addition to **2a**, cyclopentylallene **2b**, *n*-butylallene **2c** and *t*-butylallene **2d** also undergo three-component reaction with **1a** and **3** to furnish the corresponding products **4i–k** in 88, 84 and 82% yields, respectively, with high *Z* selectivity. In all cases, no trace of allylstannanes was observed. Moreover, only a single or predominantly (*Z*)-stereoisomer of allylgermane products was obtained with a *Z* : *E* ratio falling in the narrow range 94 : 6 to 99 : 1. From the above data, it seems that the stereoselectivity of the reaction is little affected by the substituent present on the allenes and aryl iodides.

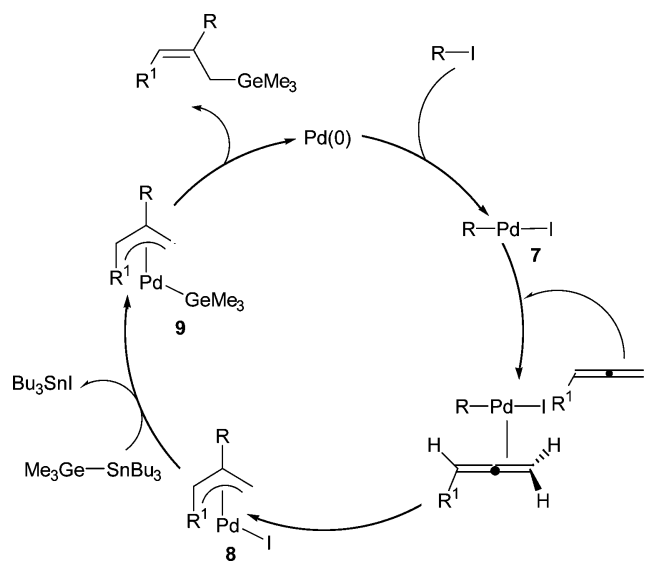
The present three-component assembling reaction can be applied successfully to a partially intermolecular coupling reaction. Treatment of allene **5** with **3** in the Pd(dba)₂–toluene system afforded chromene derivative **6** in 78% yield (Scheme 2).



Scheme 2

Based on the known palladium chemistry, a mechanism involving face-selective coordination of allene to the palladium center is proposed to account for the observed regio- and stereochemistry of products (Scheme 3). The catalytic reaction is likely initiated by the oxidative addition of aryl iodide to Pd(0) to give aryl palladium(II) intermediate **7**. The terminal double bond of allene is then coordinated favorably to the palladium center of **7** at the face opposite to the substituent R¹ to avoid steric congestion. Insertion of the coordinated double bond of the allene into the Pd–R bond affords π -allyl palladium complex **8** with the R¹ group *anti* to the R group of the π -allyl moiety. Transmetalation of **8** with stannylgermane **3** furnishes intermediate **9**. Subsequent reductive elimination of **9** affords the final product. The *anti* stereochemistry of π -allyl complex **9** accounts for the high *Z* stereoselectivity of products.

The observation of only allylgermanes **4** with no formation of allylstannanes can be attributed to the highly chemoselective transmetalation of **8** with stannylgermane **3** to form inter-



Scheme 3

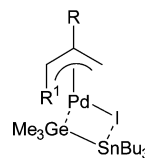


Fig. 1 Proposed cyclic S_E2 intermediate.

mediate **9**. It is likely that a cyclic S_E2 pathway is involved in the transmetalation step (Fig. 1). Such an S_E2 type mechanism has been proposed for the palladium-catalyzed Stille coupling of arylstannanes with aryl halides.¹¹ While the exact reason for the high chemoselective transmetalation is not clear, the great affinity of the –SnR₃ moiety for halide is probably the driving force for the chemoselectivity. The accompanying formation of Bu₃SnI was evidenced by the observation of the corresponding signals in the ¹H NMR spectrum of the crude reaction mixtures of **1** with **2** and **3**.^{2a}

It is to be noted that palladium-catalyzed addition of stannylgermane to allene is known in the literature.¹² However, under our standard conditions, no such addition product was observed. These results strongly indicate that the oxidative addition of Ar–I to Pd(0) is faster than that of the Ge–Sn bond.

In summary, we have developed a new phosphine-free palladium-catalyzed three-component assembly of allenes, aryl iodides and stannylgermane. This method allows an efficient synthesis of various allylgermane derivatives in good to excellent yields. The catalytic reaction is highly regio-, stereo- and chemoselective. Further work is in progress to extend the scope of this reaction to partially intermolecular coupling reactions and to study the application of these allylgermane products.

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