762 *Organometallics* **2005,** *24,* 762−764

Notes

Palladium-Catalyzed Regio- and Stereoselective Cross-Coupling of Baylis-Hillman Adducts and Bimetals: A Novel Method for the Synthesis of Substituted Allylsilanes and Allylgermanes

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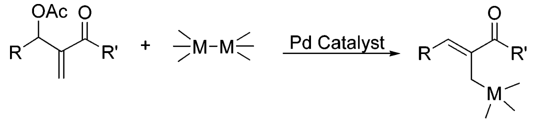
Summary: Cross-coupling reactions between Baylis-Hillman acetate adducts and bimetallic reagents (Si−Si, Ge−Ge) catalyzed by a phosphine-free palladium complex are described. 3-Substituted-2-carbonylallylsilanes and allylgermanes were isolated in high yields. The cross-coupling reactions are regio- and stereoselective.

Allylmetal reagents have found widespread use in organic synthesis.[1] Their addition to carbonyl compounds stereoselectively provides functionalized homoallylic alcohols that are used in synthesis of a variety of complex natural products. In view of their synthetic utility, the development of novel and efficient methods for preparing functionalized allylmetal reagents in a regio- and stereoselective fashion would be of great utility. In continuation of our work on boron reactions,[2] we recently reported that palladium-catalyzed coupling reactions of bis(pinacolato)diboron and Baylis-Hillman acetate adducts lead to functionalized allylborates.[3] This prompted us to examine the feasibility of coupling Baylis-Hillman acetate adducts with bimetals of both silicon and germanium (Scheme 1). The reaction would provide a convenient synthetic method for preparing a wide range of 2-carbonylallylmetal reagents that are difficult to obtain by other methods.

The Baylis-Hillman reaction is a widely employed carbon−carbon bond forming reaction.[4] It is used to convert simple starting materials into densely functionalized products that are useful in a variety of synthetic transformations. Allylsilanes are extensively used in carbonyl addition reactions[1] and coupling reactions[5] and have been employed as key intermediates in the total synthesis of natural products.[6] Allylsilanes containing a carbonyl group at the β-position (2-carbonylallylsilanes) are unique in that they can react with both electrophiles and nucleophiles.[7] Tsuji reported a preparation of allylsilanes from allyl acetates and disilanes in the presence of a palladium catalyst. Several other methods for preparing allylsilanes catalyzed by transition metals are also known,[8] but routes to 2-carbonylallylsilanes are limited.[7,9]

Scheme 1



R' = Me, OMe; M = Si, Ge

The reaction of Baylis-Hillman acetate adduct **1** and hexamethylsilane, **2** (in the presence of Pd), generates 2-methoxycarbonylallylsilanes **3** (Table 1) in high yields. A variety of catalysts and solvent systems were examined in an effort to optimize reaction conditions. Highest yields were obtained when reactions were carried out in toluene using 4 mol % of $Pd_2(dba)_3$ at 50 °C. It is noteworthy that acetates of Baylis-Hillman adducts can

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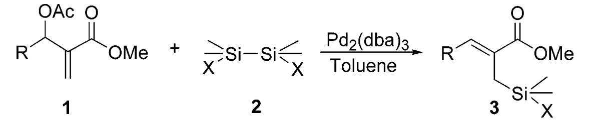
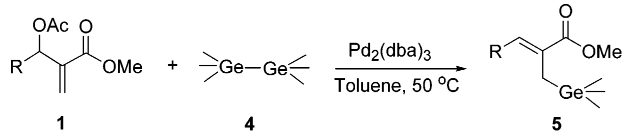
Table 1. Pd-Catalyzed Coupling of Baylis-Hillman Adduct 1 and Disilane[a]



R	X	product[b]	yield (%)[c]	Z:E[d]
phenyl	Me	**3a**	87	100
p-methylphenyl	Me	**3b**	84	96:4
p-methoxyphenyl	Me	**3c**	82	100
p-chlorophenyl	Me	**3d**	80	97:3
o-chlorophenyl	Me	**3e**	69	92:8
1-furyl	Me	**3f**	86	94:6
1-naphthyl	Me	**3g**	85	98:2
n-octyl	Me	**3h**	64	92:8[e]
phenyl	Phenyl	**3i**	73	100:0

[a] Reactions carried out for 5 h at 50 °C using 4 mol % of Pd catalyst. [b] All products exhibited satisfactory spectral (^{1}H, ^{13}C) and elemental data. [c] Isolated yields. [d] *E*/*Z* ratio determined by ^{1}H NMR. [e] Reaction time was 10 h.

Table 2. Reaction of Baylis-Hillman Adduct 1 and Hexamethyldigermanium (4) in the Presence of Pd Catalyst[a]



R	product[b]	yield (%)[c]	Z:E[d]
phenyl	**5a**	84	100
p-methylphenyl	**5b**	82	98:2
p-methoxyphenyl	**5c**	85	97:3
p-chlorophenyl	**5d**	80	92:8
o-chlorophenyl	**5e**	70	95:5
1-furyl	**5f**	81	100:0[e]
1-naphthyl	**5g**	76	100:0
n-octyl	**5h**	64	85:15[e]

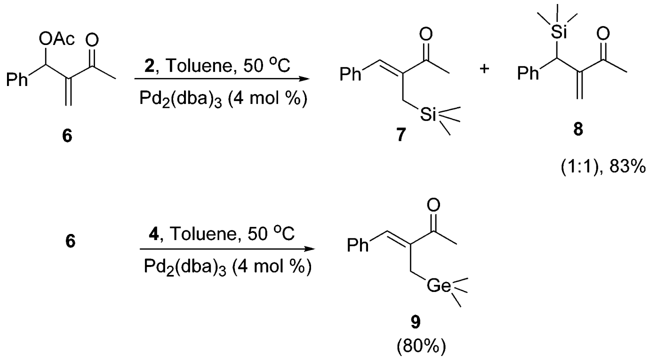
[a] Reactions carried out for 5 h at 50 °C using 4 mol % of Pd catalyst. [b] All products exhibited satisfactory spectral (^{1}H, ^{13}C) and elemental data. [c] Isolated yields. [d] *E*/*Z* ratio determined by ^{1}H NMR. [e] Reaction time was 10 h.

be silylated under mild conditions. It has been reported that allyl acetates will couple with disilanes only in the presence of chloride salt and at high temperatures,[8b,e] clearly indicating that Baylis-Hillman adducts are more reactive. Several types of Baylis-Hillman adducts readily participate in the reaction, as shown in Table 1. Baylis-Hillman adducts derived from aryl aldehydes, heteroaryl aldehydes, and aliphatic aldehydes are readily transformed into the corresponding allylsilanes.

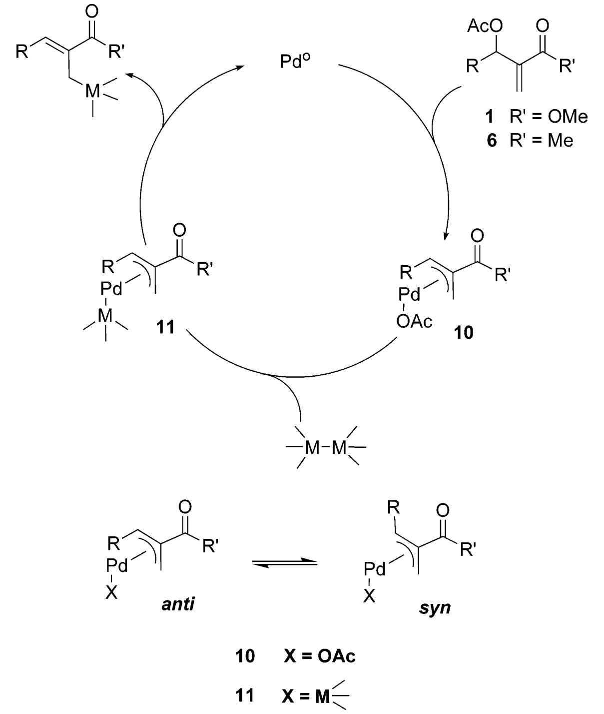
We then extended the methodology to the preparation of functionalized allylgermanes. Relative to other allylmetals, few studies focused on the synthesis of allylgermanes have been reported.[10] Notably, allylgermanes have been used in allylation reactions with carbonyl[11] and imine[12] compounds and in [3 + 2] cycloaddition[13] reactions. Baylis-Hillman acetate adduct **1** reacted with hexamethyldigermanium **4** in the presence of a Pd catalyst to form allylgermane **5** (Table 2). Reactions proceed readily at 50 °C, and the allylgermane products form in high yields. To the best of our knowledge, this is the first reported synthesis of 2-carbonylallylgermanium compounds.

Reaction of the Baylis-Hillman adduct **6** derived from methylvinyl ketone and hexamethyldisilane, **2**, gave a (1:1) mixture of (*Z*)-allylsilane **7** and its regioisomer **8**, in 83% yield, whereas the reaction of **6** with hexamethyldigermanium, **4**, yielded only **9** in 80% yield (Scheme 2).

Scheme 2



Scheme 3



The stereochemistry of the allylmetals was determined to be *Z* using ^{1}H and ^{13}C NMR spectroscopy and by comparison with the literature.[9,14] Only trace quantities of the *E* isomers were detected. The *Z* selectivity is presumably a consequence of thermodynamic control. As outlined in Scheme 3, the reaction most likely proceeds via the oxidative addition of palladium to the Baylis-Hillman adduct (**1** or **6**) to produce the π-allyl palladium complex **10**. Addition of the bimetal reagents to **10** would afford **11**, which could equilibrate (*anti* vs *syn*). Presumably the steric requirements of the carbonyl group lead to the formation of the thermodynamically

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more stable *Z*-allylmetal products that are produced by reductive elimination.

In conclusion, we have developed the palladium-catalyzed coupling of Baylis-Hillman acetate adducts with bimetallic reagents (Si–Si, Ge–Ge). The method leads to functionalized allylmetal reagents in excellent yields. The catalytic reaction proceeds with high regio- and stereoselectivity under mild conditions. Phosphine-free Pd catalyzes the reaction, and no additional base or ligand is required.

Experimental Section

General Considerations. All glassware was dried in an oven at 120 °C and flushed with dry nitrogen. Reactions were carried out under a nitrogen atmosphere. All reagents were purchase from Aldrich Chemical Co. and used as received. Baylis-Hillman adducts were prepared according to literature procedures. Products were purified by flash chromatography using silica gel (60 C, 230, 400 mesh) with hexanes and ethyl acetate (hexanes/EtOAc, 20:1) as eluent. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker 250 MHz and Varian 300 MHz instruments with chemical shifts reported relative to TMS.

General Procedure for the Synthesis of Allylsilanes 3. The Baylis-Hillman acetate adduct **1** (1 mmol) and hexamethyldisilane **2** (1.1 mmol) were added to a two-necked round-bottomed flask. The system was evacuated and purged with nitrogen gas. Toluene (4 mL) and 4 mol % of $Pd_2(dba)_3$ (36 mg) were added. The reaction mixture was stirred at 50 °C. After completion of the reaction (TLC), the mixture was concentrated and purified by column chromatography to give the desired product **3**.

General Procedure for the Synthesis of Allylgermanes 5. The Baylis-Hillman acetate adduct **1** (1 mmol) and hexamethyldigermanium **4** (1.1 mmol) were added to a two-necked round-bottom flask The system was evacuated and purged with nitrogen gas. Toluene (4 mL) and 4 mol % of $Pd_2(dba)_3$ (36 mg) were added. The reaction mixture was stirred at 50 °C. After completion of the reaction (TLC monitor), the mixture was concentrated and purified by column chromatography to give the desired product **5**.

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Supporting Information Available: ^{1}H and ^{13}C spectral and elemental analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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