Palladium-Catalyzed Hydrostannation−Cyclization of 1,6-Diynes. Generation of 1,2-Dialkylidenecyclopentanes with a Tributylstannane Moiety

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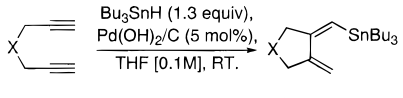
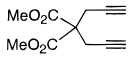
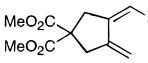
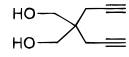
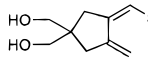
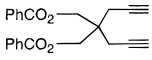
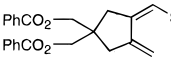
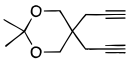
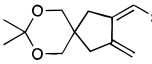
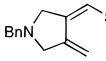
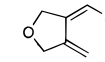
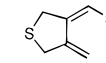
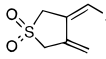
1,2-Dialkylidenecycloalkanes are useful building blocks in organic synthesis,[1] and as a result, several methods have been developed for their preparation. Among the most efficient approaches are metal-induced cyclizations of 1,*n*-enynes or diynes using Zr,[2] Ti,[3] Ni,[4] or Pd.[5] Typically, zirconium and titanium are used in stoichiometric amounts, require internal diynes ($R^1 = R^2 \neq H$), and give identically substituted exocyclic methylene groups (Y = Z), whereas nickel and palladium are catalytic in the metal, require either R^1 or R^2 to be a hydrogen, and provide unfunctionalized alkenes (Y = Z = H).[6]

We have recently reported that $Pd(OH)_2/C$ (Pearlman's catalyst) is the best catalyst for the hydrostannation of unactivated alkenes when compared to palladium catalysts that contain phosphine ligands.[7] In addition, novel chemo- and regioselectivity was observed in the hydrostannation of methylenecyclopropanes and allenes.[8,9] We now report the remarkable difference between ligandless catalysts and phosphine-containing palladium catalysts in the hydrostannation of 1,6-diynes, which generates synthetically useful 1,2-dialkylidenecyclopentanes containing a tributylstannane moiety.

Table 1. The Stannylative-cyclization of 1,6-diynes Catalyzed by $Pd(OH)_2/C$



1 2

Entry	Substrate		Product[a]		Yield (%)[b]
1		**1a**		**2a**	95
2		**1b**		**2b**	61
3		**1c**		**2c**	60
4		**1d**		**2d**	70
5		**1e**		**2e**	85
6		**1f**		**2f**	68
7		**1g**		**2g**	58[c]
8		**1h**		**2h**	77

(a) Conditions: Reactions carried out with Bu_3SnH (1.3 equiv, addition over 1 h), $Pd(OH)_2/C$ (5 mol%) in THF [0.1M]. (b) Isolated yield. (c) In addition to **2g**, the product arising from mono-hydrostannation of **1g** (with Sn terminal) was isolated in 9% yield.

Our studies began with readily available diyne **1a**, Table 1. Addition of 1.3 equiv of Bu_3SnH over 1 h (syringe pump) to a 0.1 M solution of **1a** in THF in the presence of 5 mol % $Pd(OH)_2/C$ gave the corresponding 1,2-dialkylidenecyclopentane **2a** in 95% yield as a single stereoisomer. The stannylative cyclization is applicable to a range of substrate types including those containing protected and unprotected alcohols (entries 2−4) and those with a heteroatom in the propargylic position (entries 5−8) giving in each case good to excellent yields of the corresponding cyclized products **2b**−**h**.[10,11] Of particular note is the cyclization of dipropargyl sulfide **1g** (entry 7) and sulfone **1h** (entry 8), as it has been reported that substrates containing sulfur at the propargylic position are incompatible with homogeneous palladium catalysts.[5b]

Treating **1a** with various palladium catalysts revealed several important trends. Phosphine-free catalysts such as $Pd(OH)_2/C$, Pd/C, $Pd(OAc)_2$, and $Pd_2(dba)_3$ all gave >75% yield of the cyclized product **2a**. Conversely, the use of $Pd_2(dba)_3$ in the presence of 1 or 2 equiv of PPh_3 or 1 equiv of dppb results in a complex reaction mixture containing less than 15% of the cyclized product.[12] These results suggest that a phosphine ligand occupies one of the coordination sites in a proposed Pd(II) intermediate,

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(5) (a) Trost, B. M.; Romero, D. L.; Rise, F. *J. Am. Chem. Soc.* **1994**, *116*, 4268. (b) Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255. (c) Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. J.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636. (d) Trost, B. M. *Acc. Chem. Res* **1990**, *23*, 34 and earlier references therein. (e) Grigg, R. *J. Heterocycl. Chem.* **1994**, *31*, 631 and references therein. (f) Meyer, F. E.; Ang, K. H.; Steinig, A. G.; de Meijere, A. *Synlett* **1994**, 191.

(6) For some exceptions, see: (a) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1997**, 1229. (b) Chatani, N.; Takeyasu, T.; Horiuchi, N.; Hanafusa, T. *J. Org. Chem.* **1988**, *53*, 3539. (c) Trost, B. M.; Pfrengle, W.; Urabe, H.; Dumas, J. *J. Am. Chem. Soc.* **1992**, *114*, 1923.

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(9) Lautens, M.; Ostrovsky, D.; Tao, B. *Tetrahedron Lett.* **1997**, *38*, 6343.

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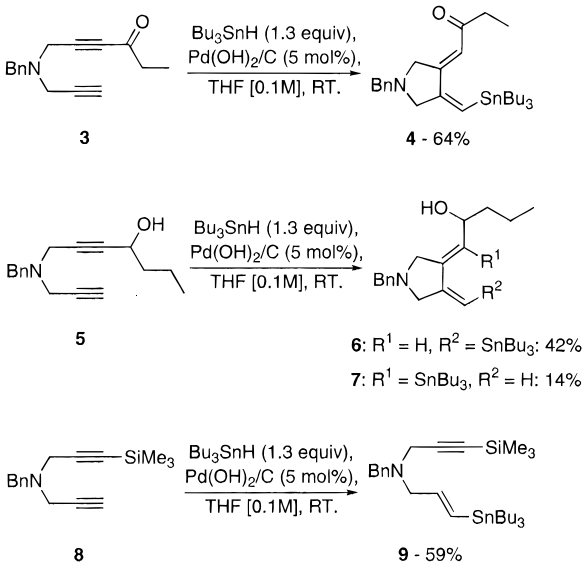
Scheme 1

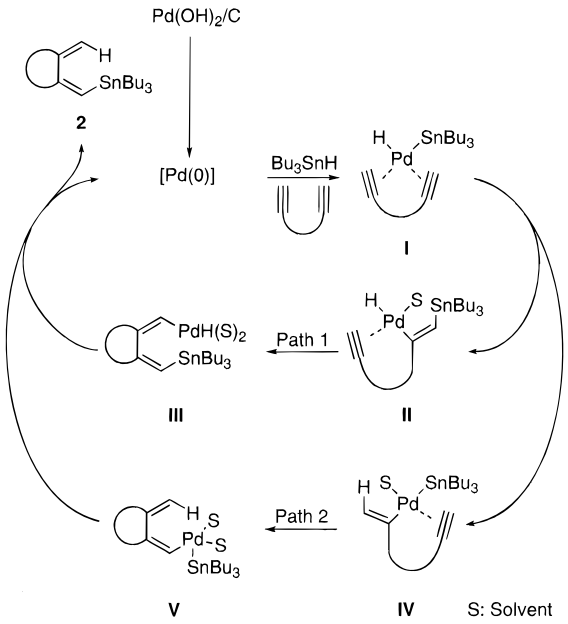


thereby preventing formation of a chelate between the diyne and the metal bearing a hydride and tributylstannyl group, *vide infra*.

Terminally substituted 1,6-diynes were also shown to undergo the cyclization although the nature of the substituent had a dramatic effect on the course of the reaction, Scheme 1.[13] Thus, alkynone **3** undergoes stannylative cyclization to furnish the α,β-unsaturated ketone **4** in 64% yield. In contrast, alkynol **5** gives a mixture of regioisomers **6** and **7** in 42% and 14% yield, respectively, pointing to electronic effects influencing the reaction pathway. Monosilylacetylene **8** undergoes regioselective hydrostannylation as the major reaction pathway to give terminal vinylstannane **9** in 59% yield (as opposed to stannylative cyclization) while the disilane gave mostly recovered starting material.

A possible catalytic cycle for the stannylative cyclization of 1,6-diynes is illustrated in Scheme 2. Thus, in those cases where a Pd(II) salt is used, reduction by Bu_3SnH may occur to give a Pd(0) species. Oxidative addition of Bu_3SnH and chelation of the 1,6-diyne leads to the key intermediate **I**, which ultimately gives the product by one of two reaction pathways.[14] Stannylpalladation of one alkyne with palladium placed so as to

Scheme 2



maintain chelation to the second alkyne leads to intermediate **II** (Scheme 2, path 1). Cyclization of **II** via carbopalladation gives **III**, which then undergoes reductive elimination to the observed product **2** while regenerating Pd(0). Alternatively, **I** may undergo a hydropalladation (**I** → **IV**), carbopalladation (**IV** → **V**), reductive elimination sequence, again leading to the same product (Scheme 2, path 2).

The synthetic utility of dienylstannanes **2** has been investigated by Diels–Alder, Stille, and transmetalation-quenching sequences, and these results will be presented in a subsequent full paper.

In summary, we have found that the choice of catalyst exerts a dramatic effect on the cyclization–stannylation of 1,6-diynes. Ligandless palladium complexes were shown to provide high yields of synthetically useful 1,2-alkylidenecyclopentanes. We are now investigating the effect of steric and electronic perturbation on the reaction pathway (hydrostannation versus stannylative cyclization).[15]

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Supporting Information Available: Experimental proceedures and compound charaterization data (11 pages).

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(10) Dienes **2a**–**d** are (*Z*)-tributylstannanes, while **2e**–**h** are (*E*)-tributylstannanes due to the change in priority at the allylic position (C vs N or O) not because of a change in reaction pathway. The (*Z*) stereochemistry of the dienylstannane portion of adduct **2a** was confirmed by the $^1H-^1H$ NOESY (compounds **2a**-**h** showed the same distinctive olefinic resonances in their ^1H and ^{13}C NMR spectra).

(11) The ^1H NMR of the crude reaction mixture for entries 1–6 and 8 indicated clean conversion to the cyclized product **2**. Although compounds **2** were isolated on Et_3N-washed silica gel, the lower isolated yields probably reflects problems with protodestannylation during column chromatography.

(12) The ^1H NMR of the crude reaction mixtures, although complex, were essentially the same and indicated that nonregioselective hydrostannylation of **1a** was the major reaction pathway (hydrostannylation:stannylative cyclization ≈ 7:1).

(13) The ^1H NMR spectra of the crude reaction mixtures indicted minor amounts of other olefin-containing products, but these could not be isolated.

(14) A palladacycle may also be proposed as an intermediate; however, this requires a Pd(IV) oxidation state.

(15) Preliminary results suggest the importance of electronic effects on the reaction pathway as *n*-butyl-substituted diyne **16** undergoes hydrostannation as the major reaction pathway (compared with stannylative-cyclization with alkynone **3**).