Efficient Conditions for the Palladium(II) Mediated Coupling of Organostannanes : The Synthesis of 1,3-Dienes, 1,4-Dienes, 1,3-Diynes and Biphenyls

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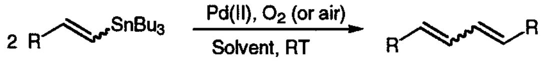
Abstract: Convenient conditions are described for the preparation of 1,3-dienes by vinylstannane homocoupling using palladium(II)-catalysis with oxygen (or air) for Pd(0)/Pd(II) reoxidation; related homo-couplings, and cross-coupling reactions with allylstannane, are used to obtain 1,3-diynes, biaryls and 1,4-dienes.

Palladium catalysed cross coupling reactions between organostannanes and organohalides (or triflates) provide a powerful method of carbon-carbon bond formation with great potential in natural product synthesis.[1] As a result of this, numerous methods have been developed for the stereospecific preparation of (*E*)- and (*Z*)-vinylstannanes.[2] Vinylstannanes have also been used to prepare symmetrical dienes *via* homocoupling reactions mediated by palladium(II)[3-6] and copper(II)[7] reagents. In the examples using palladium(II) as catalyst, *in situ* oxidation of Pd(0) to Pd(II) is required. *tert*-Butyl hydroperoxide (TBHP),[3] a copper(I)/ benzoquinone couple,[5] and HMPA[4] have all been employed for this purpose. More recently, organostannane homocoupling has been accomplished using $PdCl_2/Ph_3As$ with 1,2-dichloroethane as both the solvent and Pd(0)/Pd(II) recycling agent.[6]

During our work on the total syntheses of Alisamycin[8] and Limocrocin,[9] we discovered that the Pd(II) catalysed homocoupling of vinylstannanes can be simply carried out using oxygen (or air) to recycle the Pd(0) as shown in Scheme 1. This *Letter* reports the scope of this procedure and extensions to related cross coupling reactions.

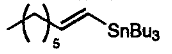
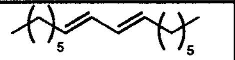
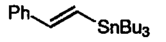
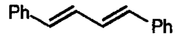
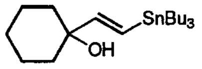
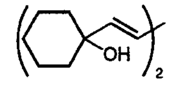
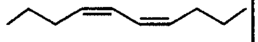
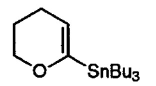
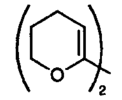


Scheme 1

Table 1 illustrates the range of substrates employed in the homocoupling process. The standard conditions employed 5 mol % of palladium(II) acetate in benzene as solvent under an atmosphere of oxygen, although air could be employed with faster coupling processes. Other solvents (*e.g.* DMF, DMSO, MeCN) and catalysts [*e.g.* $PdCl_2(MeCN)_2$] have also been employed successfully. (*E*)-1-Alkenylstannanes (entries i-iii), as well as a (*Z*)-1-alkenylstannane (entry iv), gave the corresponding dienes[10] with excellent yields and very high stereoselectivity. These reaction conditions also allowed the synthesis of Ley's *bis*-DHP protecting group[11] in good yield from the corresponding DHP-stannane (entry v). In addition, arylstannanes (entry vi) and arylethynylstannanes (entry vii) are converted smoothly into their respective symmetrical dimers in high yields. The dimerisation of tributylstannylpentyne was also investigated, but the dimer was obtained but in relatively poor yield (*ca.* 35%). This new procedure, which is experimentally simple and avoids toxic reagents and solvents, has proved to be as efficient and general as published methods. In addition, a reductive work-up procedure is not required and, in many cases, the reaction mixture can be simply concentrated under reduced pressure and the crude product purified chromatographically.

Oshima *et al.* have described Pd(II) catalysed cross coupling reactions between vinylstannanes and allylstannanes using $TBHP/Pd(OAc)_2$.[3] We have shown that similar coupling reactions can also be carried out using oxygen to recycle the Pd(0) catalyst and produce a range of 1,4-dienes (Scheme 2 and Table 2).

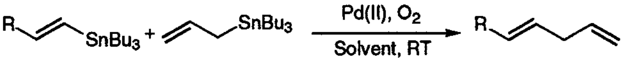
Table 1. Homocoupling reactions[a]

Entry	Substrate	Product	Yield[a]
i			79%
ii			78%
iii			86%[b]
iv			76%
v			76%
vi	$Ph{-}SnBu_3$	Ph–Ph	92%[b]
vii	$Ph{-}C{\equiv}C{-}SnBu_3$	$Ph{-}C{\equiv}C{-}C{\equiv}C{-}Ph$	89%[c]

[a] Carried out on *ca.* 1 mmol scale in benzene with 5% $Pd(OAc)_2$ and O_2 unless otherwise noted. Reactions were monitored by TLC and took 1-8 h. Yields are of chromatographed material (corrected for tin impurities).

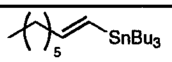
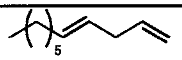
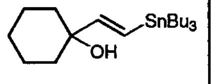
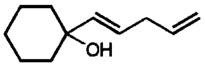
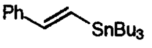
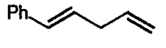
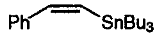
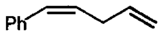
[b] These reactions were carried out using 5% $PdCl_2(MeCN)_2$/DMF/air.

[c] DMSO as solvent.



Scheme 2

Table 2. Cross coupling of vinylstannanes with allylstannane[a]

Entry	Substrate	Product	Yield[a]
i			94%[b]
ii			72%[b]
iii			84%
iv			75%
v			73%

[a] Carried out on *ca.* 1 mmol scale in benzene with 5% $Pd(OAc)_2$ and O_2 unless otherwise noted. Reactions were monitored by TLC and took 1-18 h. Yields are of chromatographed material (corrected for tin impurities).

[b] These reactions were carried out using 5% $PdCl_2(MeCN)_2/DMF/O_2$.

As can be seen from Table 2, both (*E*)-vinylstannanes (entries i-iii) and (*Z*)-vinylstannanes (entries iv, v) lead to the corresponding 1,4-dienes in good to high yield with complete stereoselectivity. In these examples, the amount of homocoupled diene did not exceed 10%. However, in the attempted allylation of aryl and arylalkynylstannanes, only moderate yields of the adducts (*ca.* 30%) were obtained due to the rapid dimerisation of the starting stannanes. In these two cases, the dimerisation process could probably be minimised by using a greater excess of allylstannane or by slow addition of the substrate to allylstannane and the catalyst.

In both types of reaction (Tables 1 and 2), the precipitation of variable amounts of palladium black was observed. This can be a problem with large scale reactions in particular; we found that the problem could be minimised by adding the catalyst (5 to 15 mol %) in 3 or 4 portions depending on the reaction progress.

In summary, we have developed an improved, straightforward procedure for the palladium(II) catalysed homocoupling of vinyl, aryl and alkynyl stannanes. In addition, this procedure has been applied to the cross coupling of vinylstannanes with allylstannane to give 1,4-dienes in good yield and with high stereoselectivity.

Representative procedure

A solution of the stannane (1 mmol) in benzene (4 mL), previously saturated with oxygen (or air for facile couplings), was treated with palladium(II) acetate (12 mg, 5 mmol %) at room temperature with efficient magnetic stirring. The reaction was kept under an oxygen atmosphere and monitored by TLC. After disappearance of the starting material (1-18 h), the reaction mixture (a black suspension) was diluted with ether and washed with water. The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (still containing palladium black) was purified by silica gel chromatography to afford the desired dimer. A similar procedure was followed for cross coupling but with the addition of allylstannane (662 mg, 2 mmol) at the start of the reaction.

(*E,E*)-1,1'-Buta-1,3-dienediyl-bis-cyclohexanol (Table 1, entry iii):

Obtained in 86% yield as a white solid, m.p. 110-111°C (Lit.[12] m.p. 115-116°C); R_f 0.18 (SiO_2, light petrol-EtOAc, 7:3), which gave consistent IR, ^{1}H-NMR and ^{13}C-NMR spectra; MS (EI) *m/z* 250 (M^+, 4%), 232 (100), 151 (37), 133 (21), 81 (68); [HRMS (EI) 250.1940. $C_{16}H_{26}O_2$ requires 250.1933 (3 ppm error)].

(*E*)-1-(1',4'-Pentadienyl)cyclohexanol (Table 2, entry ii):

Obtained in 72% yield as a colourless oil; R_f 0.54 (SiO_2, light petrol-EtOAc, 7:3); IR (NaCl, cm^{-1}) 3395, 2932, 2855, 1637, 1447, 973, 911; ^{1}H NMR (500 MHz, $CDCl_3$) 5.83 (1H, ddt, *J* 17.5 10.5, 6.5 Hz), 5.69 (1H, dt, *J* 16.0, 6.5 Hz), 5.61 (1H, dt, *J* 16.0, 1.5 Hz), 5.05 (1H, ddt, *J* 17.5, 1.5, 1.5 Hz), 5.00 (1H, ddt, *J* 10.5, 1.5, 1.5 Hz), 2.79 (2H, tq$_{app}$, *J* 6.5, 1.5 Hz), 1.74-1.47 (8H, m), 1.42-1.23 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) 138.9, 136.8, 125.5, 115.2, 71.2, 38.0, 36.3, 25.5, 22.1; MS (EI), *m/z* : 166 (M^+, 14%], 148 (5), 125 (100), 112 (22), 95 (82), 81 (50); [HRMS (EI) 166.1364. $C_{11}H_{18}O$ requires 166.1358 (4 ppm error)].

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