Palladium Catalysed Direct Allylation of Pronucleophiles with Allylstannanes

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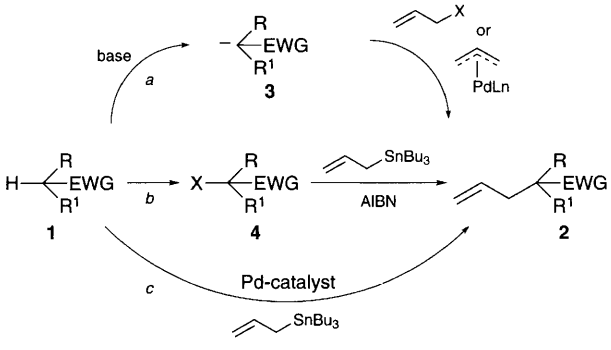
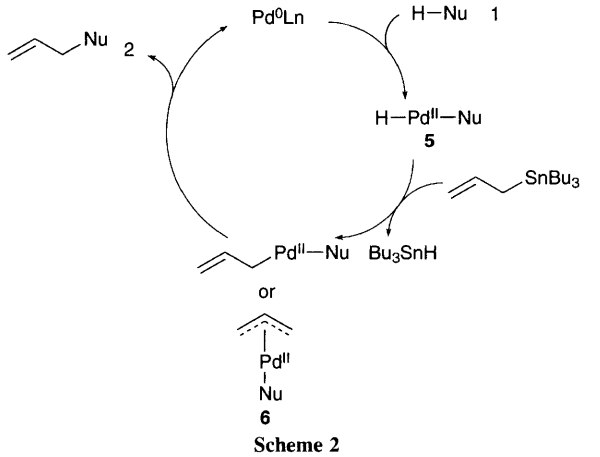
The reaction of pronucleophiles **1** with allyltributylstannanes in the presence of catalytic amounts of $Pd_2(dba)_3{\cdot}CHCl_3$ (4 mol%) and 1,2-bis(diphenylphosphino)ethane (dppe) (10 mol%) at room temperature gives the corresponding allylation products in good to high yields.

Conversion of pronucleophiles **1** to the corresponding allylated derivatives **2** has been carried out, generally, *via* the carbanion process (*a*) or the free-radical chain procedure (*b*). Pronucleophiles **1** are first converted to the corresponding carbanions **3**, which are treated either with allyl halides (or related allylic compounds) or with allyl palladium complexes [path (*a*)].[1] The reaction of allyltributylstannane with reactive halides **4**, which are obtained from pronucleophiles **1** *via* halogenation, in the presence of AIBN affords the allylated derivatives **2** [path (*b*)].[2] Here we report an entirely new procedure which enables the direct conversion of **1** to **2** [path (*c*)]; reaction of compound **1** with allylic stannanes in the presence of catalytic amounts of $Pd_2(dba)_3{\cdot}CHCl_3$ at room temperature gave compound **2** in high to good yields (Scheme 1).†

The results are summarised in Table 1. The reaction of methylmalononitrile **1a** with allyltributyltin (2 equiv.) in the presence of 4 mol% $Pd_2(dba)_3{\cdot}CHCl_3$ and 10 mol% dppe in CH_2Cl_2 at room temperature gave the allylated product **2a** in 86% yield (entry 1). The reaction of **1a** with but-2-enyltributyltin (2 equiv.) under similar conditions as above afforded a 57:43 mixture of straight **2b** and branched **2b′** butenylation products in 98% combined yield (entry 2). Similarly, the reactions of ethyl 2-cyano-2-phenylacetate **1b** with allyltin or but-2-enyltin gave the allylated **2c** or butenylated (**2d** and **d′**) products, respectively, in high yields (entries 3 and 4). Methallyltributyltin also reacted with compound **1b** to give the corresponding methallyl derivative **2e** in 66% yield (entry 5). Not only pronucleophiles bearing CN substituents (**1a, b**) but also those having ester and ketone groups (**1c–f**) underwent direct allylation in the presence of the palladium catalyst to afford allylation products (**2f–i**) (entries 6–9). (*R*)-BINAP (5 mol%) was used as a ligand, instead of dppe, in the reactions of compounds **1b** and **1c** with allyltributyltin, and higher chemical yields were achieved; 92% yield of **2c** (*cf.* entry 3) and 76% yield of **2f** (*cf.* entry 6). Other catalysts were examined in the reaction of **1b** with allyltributyltin (*cf.* entry 3); the use of 8 mol% $PdCl_2(MeCN)_2$ or $PdCl_2(PhCN)_2$ gave **2c** in 76–81% yields. Normally, the allylation was performed with 2 equiv. of allyltin for 2 d, but with **1a**, **2a** was obtained in 86% yield with 1.1 equiv. allyltributyltin after only 1 d.



Scheme 1



Scheme 2

Not only methynes but also activated methylenes underwent allylation to give the diallylation products in acceptable yields (entries 10–12). No mono-allylation products were obtained even using 1 or 2 equiv. of allyltin. The mono-allylation product **2m** was produced selectively in the case of **1j** (entry 13).

A mechanistic rationale which accounts for the unprecedented direct allylation of pronucleophiles **1** is shown in Scheme 2. The oxidative insertion of Pd^0 into the C–H bond of pronucleophiles **1** would produce the Pd^{II} intermediate **5**.[3] Transmetallation between **5** and allyltributyltin would give the π-allylpalladium–Nu (or σ-allyl) complex **6** and tributyltin hydride. Reductive coupling from **6** may produce **2** and Pd^0. We followed the reaction of **1b** with allyltributyltin in $CDCl_3$ using ^1H NMR spectroscopy and found that a signal at δ 5.28 ascribed to $HSnBu_3$ appeared clearly along with the signals due to the allylation product. Accordingly, it is most probable that the proposed transmetallation process is involved in the catalytic cycle. One may consider a possibility that the allyltributylstannane reacts with the palladium complex to produce a π-allylpalladium species which undergoes nucleophilic attack of Nu^-.‡ In an NMR tube, $Pd_2(dba)_3{\cdot}CHCl_3$ (1 equiv.) and 10 mol% dppe were dissolved in $CDCl_3$, and then allyltributyltin (1 equiv.) was added at room temperature. Even after 19 h, signals due to the allyltin remained unchanged, suggesting that no reaction takes place between the palladium catalyst and allyltin at room temperature in the absence of pronucleophiles. The signals of allyltin disappeared by heating the mixture at 50 °C for 9 h, and those ascribed to a π-allylpalladium species appeared.§ Then, **1b** (1 equiv.) was added at room temperature, but no allylation product was obtained even after 2 d.

The direct allylation[4] of pronucleophiles proceeds under essentially neutral conditions at room temperature (except entry 9). This unprecedented reaction proceeds *via* a facile transmetallation producing Bu_3SnH and **2**.

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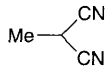
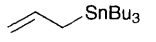
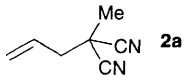
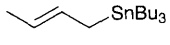
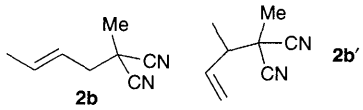
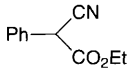
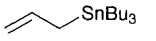
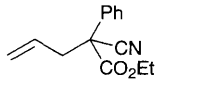
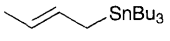
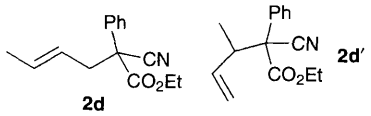
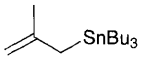
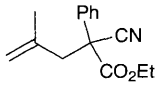
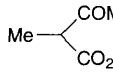
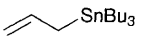
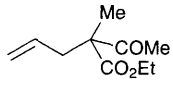
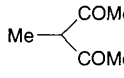
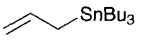
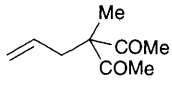
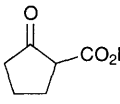
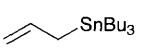
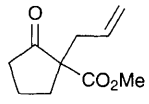
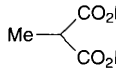
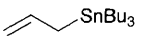
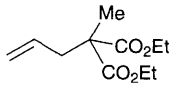
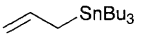
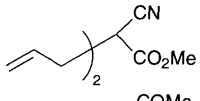
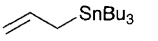
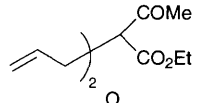
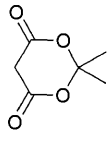
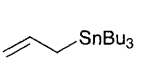
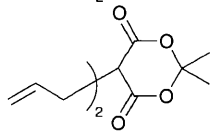
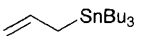
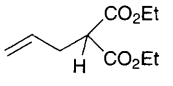
Footnotes

† *General procedure* for the direct allylation. Dry CH_2Cl_2 (1 ml) and $Pd_2(dba)_3{\cdot}CHCl_3$ (0.02 mmol) were placed in a flask under an Ar atmosphere. Pronucleophiles (0.5 mmol) were added with stirring at room temperature, and then allyltributyltin (1 mmol) was added. The mixture was then stirred for 2 d at room temperature and the palladium complex removed by filtration with celite. The product was purified by silica gel column chromatography using hexane–ethyl acetate (30:1) as eluent.

Table 1 Palladium catalysed direct allylation of pronucleophiles **1**[a]

Entry	Pronucleophiles **1**	Allylstannanes (2 equiv.)	Product	Isolated yield (%)
1	 **1a**		 **2a**	86
2	**1a**		 **2b** **2b′**	98[b]
3	 **1b**		 **2c**	89
4	**1b**		 **2d** **2d′**	90[c]
5	**1b**		 **2e**	66
6	 **1c**		 **2f**	65[e]
7	 **1d**		 **2g**	65[e]
8	 **1e**		 **2h**	70
9	 **1f**		 **2i**	20[d]
10	 **1g**		 **2j**	50[f,g]
11	 **1h**		 **2k**	41[f,g]
12	 **1i**		 **2l**	45[f,g]
13	 **1j**		 **2m**	47[f,h]

[a] A mixture of **1** (0.5 mmol), allyltin (1 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.02 mmol), dppe (0.05 mmol), and dry CH_2Cl_2 (1 ml) was stirred at room temp. for 2 d under Ar, except where otherwise indicated. [b] **2b** : **2b′** = 57 : 43. [c] **2d** : **2d′** = 53 : 47. [d] Since the reaction at room temp. was sluggish, THF was used as a solvent and the mixture was refluxed overnight. The allylation product **2i** was isolated in 20% yield along with the recovered **1f** (43%). [e] The starting materials **1c** and **1d** were recovered in 11% yields. [f] 4 equiv. of allyltributylstannane were used. [g] No mono-allylation product was obtained even using 2 equiv. of allyltin. [h] No di-allylation product was obtained even using 4 equiv. of allyltin.

‡ In this case, abstraction of a proton from H–Nu by a base is required. However, no base is present in the reaction medium. An additive such as dppe is not a strong enough base to abstract the hydrogen.

§ At room temperature, broad signals appeared around olefinic region because of its fluxional character. At −60 °C, those signals changed to sharp signals characteristic of π-allyl structure.

References

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