Unprecedented highly chemoselective allylation of imines in the presence of aldehydes *via* a palladium catalysed allylstannane reaction

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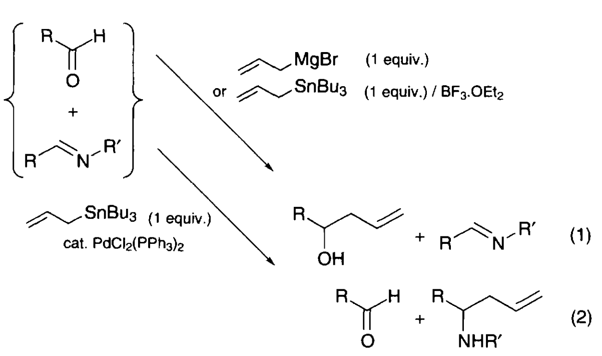
Imines are allylated chemoselectively in the presence of aldehydes using allylstannanes with a π-allylpalladium chloride dimer catalyst.

It is widely accepted by organometallic and organic chemists that an aldehyde is more reactive towards carbanionic organometallics, such as allyl Grignard and allyllithium reagents, than the corresponding imine, [eqn.(1)]. This is also the case in the Lewis acid mediated allylation with allylstannanes and allylsilanes[1] [eqn.(1)]. Here we report that an entirely opposite chemoselectivity can be obtained by the palladium catalysed reaction of allylstannanes, [eqn.(2)]; an imine is more reactive than the corresponding aldehyde under such conditions.

We recently reported that the palladium (and platinum) catalysed addition of allylstannanes with aldehydes proceeds through a bis-π-allylpalladium intermediate, which acts as a nucleophilic allylating agent.[2] The nucleophilic reactivity of the intermediate is in marked contrast to the electrophilic reactivity of ordinary π-allylpalladium complexes (π-allylPdX, X = OAc, halogen,OCO_2R *etc.*).[3] We first extended this finding to the imine addition reaction (Table 1). The addition of allyl- (**1a**), crotyl- (**1b**) and methylallyl- (**1c**) stannanes to various imines (**2a–g**) proceeded smoothly to give the corresponding allylated products **3** in good to high yields. Surprisingly, the reactivities of allylstannanes to imines were higher than those to aldehydes.†,[2] We next examined the palladium catalysed allylation in the presence of both aldehydes and imines [eqn. (3) and Table 2].

Generally speaking, the reactivity of allylstannanes to aldehydes is higher than that to imines under Lewis acid promoted conditions (methods B and C).[1] However, the allylation chemoselectivity under the palladium catalysed conditions was completely reversed; the highest selectivities were especially obtained using a π-allylpalladium chloride dimer as catalyst (method A).‡ Reasonably high chemoselectivity was obtained in the allylation of *p*-nitrobenzaldehyde and its amine partner **2a**, derived from methyl *p*-aminobenzoate (the Ciufolini imine[4]) (entries 1 and 2). The use of imine derived from aniline decreased the chemoselectivity (entries 3 and 4). Very high chemoselectivities were produced in the allylation of other aromatic, aliphatic and cinnamic aldehydes and their imine partners (entries 5–14). The use of the Ciufolini imine was essential to obtain such high chemoselectivities. We also examined the allylation with allylmagnesium bromide in the presence of *p*-nitrobenzaldehyde and **2h** (1 : 1) to elucidate the chemoselectivity in a carbanionic allylation; **3**:**5** = 1 : >99 (*cf.* entries 3 and 4).

This unprecedented chemoselectivity can be explained by the difference of the coordination ability between the nitrogen and oxygen atoms to the transition metal (Scheme 1). In general, a nitrogen atom can coordinate to a transition metal more strongly than an oxygen atom.[5] Catalytic amounts of the bis-π-allylpalladium intermediate **6** would react with imines more predominantly than with aldehydes to give **7**, which would afford **3** *via* **8**. The key intermediate **6** is regenerated by the reaction of **8** and **1a**. Excess amounts of Lewis acid (> 2 equiv.) can coordinate to both aldehyde and imines, activating both electrophiles in the same manner; the resulting aldehyde–Lewis acid complex is more electrophilic than the imine complex. The use of 1 equiv. $BF_3{\cdot}OEt_2$ (Table 2) gave *ca.* 50 : 50 of **3** to **5** and the use of catalytic (10 mol%) $BF_3{\cdot}OEt_2$ did not give the allylation products at all.[6] The regeneration of **6** *via* the catalytic



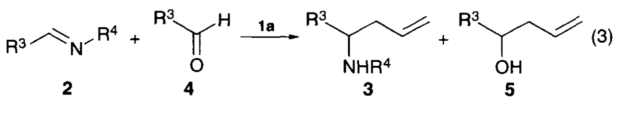
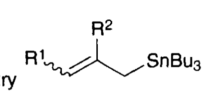
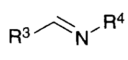
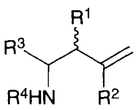


Table 1 Palladium catalysed allylation of allylic stannanes with imines[a]

Entry	 **1**	 **2**	Reaction time	 **3**, yield (%)
1	**a** $R^1 = R^2 = H$	**a** $R^3 = p\text{-}(NO_2)C_6H_4$ $R^4 = p\text{-}(CO_2Me)C_6H_4$	1 d	77
2	**a**	**b** $R^3 = p\text{-}(NO_2)C_6H_4$ $R^4 = Bn$	1 d	98
3	**a**	**c** $R^3 = Ph$ $R^4 = p\text{-}(CO_2Me)C_6H_4$	2 d	98
4	**a**	**d** $R^3 = p\text{-}(OMe)C_6H_4$ $R^4 = p\text{-}(CO_2Me)C_6H_4$	2 d	82
5	**a**	**e** $R^3 = PhCH = CH$ $R^4 = p\text{-}(CO_2Me)C_6H_4$	20 h	90
6	**a**	**f** $R^3 = c\text{-hex}$ $R^4 = p\text{-}(OMe)C_6H_4$	2 d	72
7	**a**	**g** $R^3 = Pr^i$ $R^4 = p\text{-}(CO_2Me)C_6H_4$	14 h	81
8	**b** $R^1 = Me$ $R^2 = H$	**a**	1 d	96(6:4)[c]
9	**b**[b]	**b**	18 h	76(1:1)
10	**c** $R^1 = H$ $R^2 = Me$	**g**	20 h	80

[a] A mixture of **1** (0.6 mmol), **2** (0.5 mmol), $PdCl_2(PPh_3)_2$ (0.05 mmol) and THF (5 ml) was stirred at 50 °C for the indicated period. [b] Crotylstannane, *E*:*Z* = 76 : 24, was used. [c] *Syn* : *anti* shown in parentheses. Crotylstannane, *E*:*Z* = 60 : 40, also produced the adduct in 94% yield with same *syn* : *anti*.

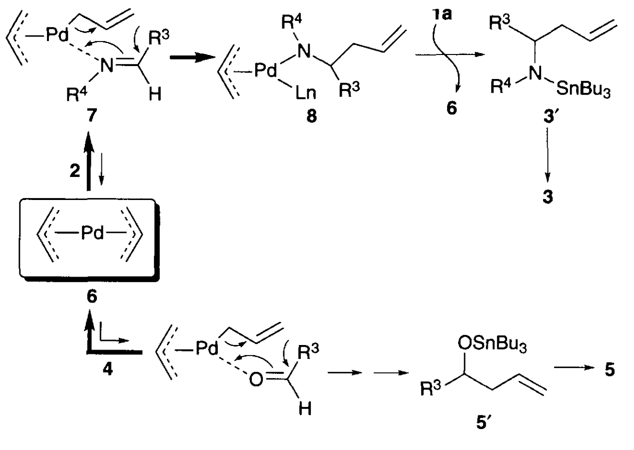
Table 2 Chemoselective allylation of imines in the presence of aldehydes

Entry	Imine 2	Aldehyde **4**	Conditions^a	Yield (%)	**3**:**5**^{b}
1	**a**	p-$(NO_2)C_6H_4CHO$	A	90	90:10
2			B	95	10:90
3	**h**^{c}	p-$(NO_2)C_6H_4CHO$	A	84	83:17
4			B	91	19:81
5	**d**	p-$(MeO)C_6H_4CHO$	A	99	97:3
6			B	96	1:>99
7	**i**^{c}	*p*-tolualdehyde	A	86	94:6
8			B	99	5:95
9	**e**	*trans*-cinnamaldehyde	A	99	>99:1
10			B	98	1:>99
11	**f**	*c*-hexylcarboxaldehyde	A	80	91:9
12			C	60	1:>99
13	**j**^{c}	*c*-hexylcarboxaldehyde	A	99	>99:1
14			C	60	1:>99

^{a} A; A mixture of **2** (0.2 mmol), **4** (0.2 mmol) and allyltributylstannane (0.2 mmol) was dissolved in THF (5 ml). $(\eta^3\text{-}C_3H_5PdCl)_2$ (0.02 mmol, 10 mol%) was then added at room temp. and the mixture was stirred until a black suspension was formed; B and C; A mixture of **2** (0.2 mmol), **4** (0.2 mmol) and allyltributylstannane (0.2 mmol) was dissolved in CH_2Cl_2 (5 ml). To the mixture was added $BF_3{\cdot}OEt_2$ (0.8 mmol) (method B) or $SnCl_4$ (method C) at −78 °C and the mixture was stirred for 1 h. ^{b} Ratios were determined by ^1H NMR. ^{c} The imine structures are as follows; **2h**; p-$(NO_2)C_6H_4CH{=}NPh$, **2i**; p-$MeC_6H_4CH{=}N(p\text{-}CO_2MeC_6H_4)$, **2j**; c-$hexCH{=}N(p\text{-}CO_2MeC_6H_4)$.

process in addition to the strong coordinative preference of the nitrogen atom are key steps in this unusual chemoselectivity; the Lewis acid promoted reaction never proceeds *via* a catalytic process.

Consequently, both the Pd-coordination characteristics and the catalytic cycle produce the unusual chemoselectivity. Irrespective of the precise mechanism, the reversed chemoselectivity is synthetically useful.



Scheme 1

Footnotes

† The reactivity of crotylstanane **1b** was typical. The reaction of **1b** with benzaldehyde gave the adduct in only 37% yield after 4 d at room temp., whereas the reaction with the corresponding imine afforded the allylated amine in essentially quantitative yield.

‡ $PdCl_2(PPh_3)_2$, which was used in the allylation shown in Table 1, also worked in the chemoselective allylation, but $(\eta^3\text{-}C_3H_5PdCl)_2$ gave better results.

References

1 Y. Yamamoto and N. Asao, *Chem. Rev.*, 1993, **93**, 2207, and references cited therein.

2 H. Nakamura, N. Asao and Y. Yamamoto, *J. Chem. Soc., Chem. Commun.*, 1995, 1273.

3 Tsuji *et al.*, reported a bis-π-allylpalladium intermediate, generated by palladium catalysed dimerization of butadiene, which reacted with aldehydes; K. Ohno, T. Mitsuya and J. Tsuji, *Tetrahedron.*, 1972, **28**, 3705 and references cited therein.

4 M. A. Ciufolini and G. O. Spencer, *J. Org. Chem.*, 1989, **54**, 4739; For transition metal catalysed addition of pronucleophiles to the imines, see Y. Yamamoto, Y. Kubota, Y. Honda, H. Fukui, N. Asao and H. Nemoto, *J. Am. Chem. Soc.*, 1994, **116**, 3161.

5 *Principles and Applications of Organotransition Metal Chemistry*, ed. J. P. Collman, L. S. Hegedus, J. R. Norton and R. G. Finke, University Science Books, Mill Valley, 1987, pp. 57–66.

6 Normally, more than 1 equiv. Lewis acid is needed for the allylation of aldehydes or imines using allylstannanes and silanes.[1] Quite recently, catalytic allylation of imines promoted by lanthanide triflates has been reported; C. Bellucci, P.Cozzi and A. Umani-Ronchi, *Tetrahedron Lett.*, 1995, **36**, 7289. However, the chemical yields (30–70%) were generally low in the catalytic system.

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