Palladium–indium mediated Barbier-type allylation of aldehydes with allenes

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A new allylation reaction of carbonyl compounds using allenes is described; homoallylic alcohols were obtained in moderate to good yields from aryl iodides, allenes and carbonyl compounds and an excellent diastereoselection was exhibited when 2-hydroxycyclohexanone was employed.

In the last decade indium has emerged as the metal of choice to mediate the allylation of carbonyl compounds because of its environmentally benign properties allied with a high degree of *chemo*-, *regio*- and *diastereo*-selectivity especially in aqueous media.[1] Furthermore the reaction requires no activation of the carbonyl group and produces few by-products.

The indium mediated allylation reaction is an aldol-type reaction where the nucleophile is an allylindium(I) species usually generated from an allylic halide and indium(0).[2]

Here, we describe the formation of allylindium species by transmetallation[3] of π-allylpalladium(II) complexes generated from aryl iodides and allenes. The resultant allylindium species subsequently add to the carbonyl compound affording homoallylic alcohols (Scheme 1).

There are four synthetic variants of this Pd–In mediated reaction depending on whether the Pd or the In step are *intra*- or *inter*-molecular.

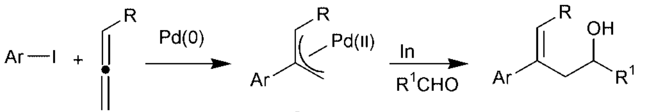
A first set of examples (class 1 processes) where both the Pd and the In steps are intermolecular is presented in Table 1. Aryl/heteroaryl iodides (1.5 mmol) react (DMF, 80 °C, 18 h, Schlenk tube) with allene (1.0 bar) and aldehydes (1.0 mmol) in the presence of indium (100 mesh powder, 1.5 mmol), $Pd(OAc)_2$ (0.1 mmol) and tris(2-furyl)phosphine (0.2 mmol). The use of triphenylphosphine resulted in an incomplete conversion of the starting materials.

Encouraged by these results we employed a substituted allene, *n*-octylallene[4] (1.5 mmol) in the process. A reaction time of 24 h was necessary to achieve complete conversion of the aldehyde. In both the cases so far explored (Table 2) only one geometric isomer was produced and their structures were assigned from NOE data.

A class 2 process (intermolecular π-allyl formation—intramolecular allylation[5]) was explored next. The increased rigidity of the transition state of the aldol-like addition (sub-optimal approach trajectory) may explain the lower yield observed in entry 1. The six membered product was obtained in a better yield (Table 3). The catalytic system comprised $Pd(PPh_3)_4$ (10 mol%) (entry 1) or $Pd_2(dba)_3$ (5.0 mol%) and tris(2-furyl)phosphine (20.0 mol%) (entry 2).

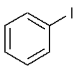
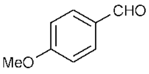
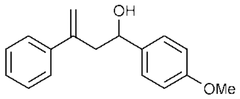
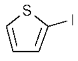
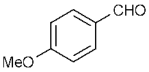
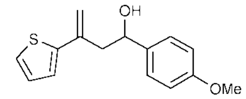
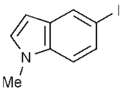
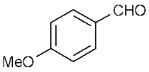
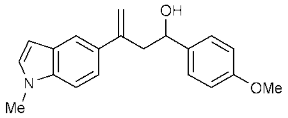
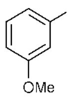
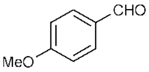
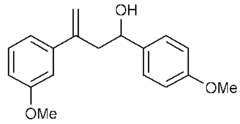
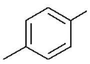
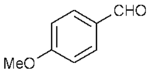
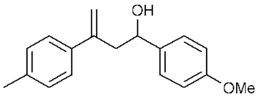
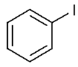
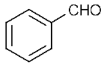
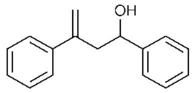
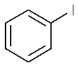
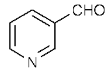
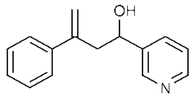
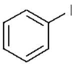
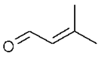
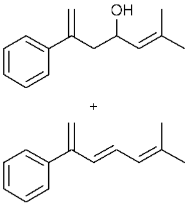
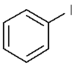
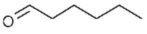
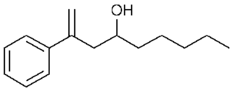
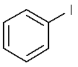
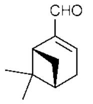
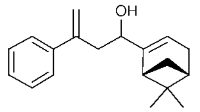
A class 3 process requires an aryl/heteroaryl iodide bearing an allenic side chain. The Pd catalysed step is then intramolecular and is combined with an intermolecular In mediated reaction. Allenyl (2-iodobenzyl) ether[7] (1.0 mmol) was reacted (DMF, 90 °C, 14 h) with aldehydes (1.05 mmol) in the presence of $Pd(PPh_3)_4$ (0.10 mmol) (Scheme 2).

We have briefly studied the effect of chelating groups α to the carbonyl group, such as nitrogen,[8] hydroxyl[9] and alkoxy,[10] on the stereochemical outcome (Table 4) of the reaction of iodobenzene and allene following the protocol described above.



Scheme 1

Table 1

Aryl iodide	Aldehyde	Product	Yield (%)
			64
			66
			64
			60
			40
			43
			65
			70[a]
			65
			47[b]

[a] Alcohol : triene 2 : 1 (^{1}H NMR); [b] 1 : 1 Mixture of diastereoisomers (^{1}H NMR).

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Table 2

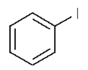
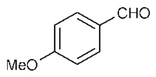
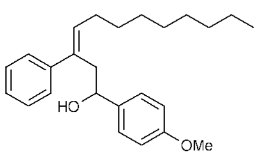
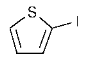
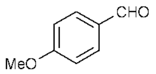
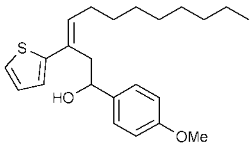
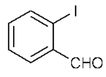
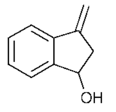
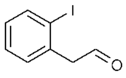
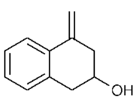
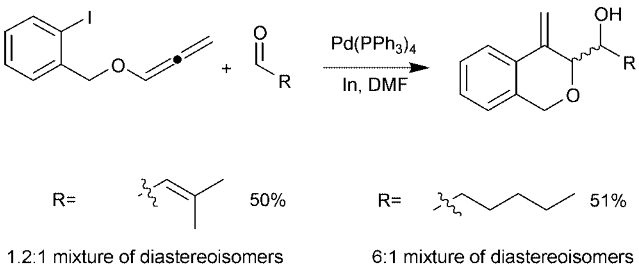
Aryl iodide	Aldehyde	Product	Yield (%)
			50
			54

Table 3

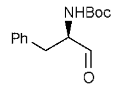
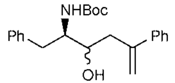
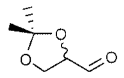
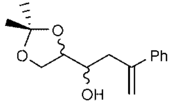
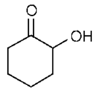
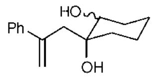
Aldehyde	Product	Yield (%)
		37
		48[6]

The preliminary results (Table 4) show that the palladium–indium mediated allylation of carbonyl compounds using allenes provides easy access to homoallylic alcohols and that chelation clearly controls its diastereoselectivity.



Scheme 2

Table 4

Reagent	Product	*Syn* : *Anti*[a]	Yield (%)
		1 : 1	75
		5 : 1[b]	55
		96 : 4	67

[a] Determined by ^{1}H NMR prior to purification. [b] X-Ray analysis on the major isomer in progress.

Further work on these and on the related class 4 processes (intramolecular π-allyl formation—intramolecular aldol-like condensation) are in hand.

We thank the EPSRC and Leeds University for support.

Notes and references

1 C. J. Li and. T. H. Chan, *Tetrahedron*, 1999, **55**, 11 149.
2 T. H. Chan and Y. Yang, *J. Am. Chem. Soc.*, 1999, **121**, 3228.
3 J. A. Marshall and C. M. Grant, *J. Org. Chem.*, 1999, **64**, 8214.
4 S. Searles, L. Yushun, B. Nassim, M. T. Robert-Lopes, P. Tran and P. Crabbè, *J. Chem Soc., Perkin Trans. 1*, 1984, 747.
5 To our knowledge this is the only example of In mediated intramolecular Barbier reaction: L. A. Paquette and J. L. Mendez-Andino, *J. Org. Chem.*, 1998, **63**, 9061.
6 S. E. Gibson, N. Guillo, R. J. Middleton, A. Thuilliez and M. J. Tozer, *J. Chem Soc., Perkin Trans. 1*, 1997, 447.
7 R. Grigg and J. M. Sansano, *Tetrahedron*, 1996, **52**, 13 441.
8 L. A. Paquette, T. M. Mitzel, M. B. Isaac, C. F. Crasto and W. W. Schomer, *J. Org. Chem.*, 1999, **62**, 4293.
9 L. A. Paquette and P. C. Lobben, *J. Org. Chem.*, 1998, **63**, 5604.
10 L. A. Paquette and P. C. Lobben, *J. Am. Chem. Soc.*, 1996, **118**, 1917.