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A novel palladium-catalyzed coupling of epoxides with allyl bromide mediated by indium(I) chloride: a cascade epoxide rearrangement–carbonyl allylation†

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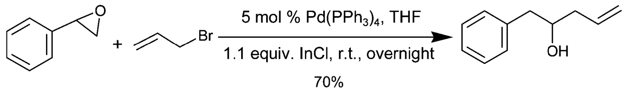
A cascade epoxide rearrangement–aldehyde allylation was developed by using a combination of InCl and reusable heterogeneous mesoporous silica supported palladium catalysts.

Allylation of aldehydes is an important transformation in organic synthesis.[1] Over the past decade, allylation reactions by allylic indium reagents, in particular, have been of increasing interest because of their tolerance to water, which allows their wide uses in aqueous media for environmentally benign syntheses.[2] Generally, the allylindium reagent can be prepared by the conventional transmetalation of allyllithium or allyl Grignard reagents with indium(III) halides,[3] by the oxidative addition of metallic indium[4] or indium(I) iodide[5] to allylic substrates, or by the reductive transmetalation of π-allylpalladium(II) with indium(I) salts.[6] In connection with our interest in the synthetic application of allylindium reagents, we have investigated the coupling reaction of epoxides with allylindium reagents, generated *in situ* from reductive transmetalation of π-allylpalladium(II) with indium(I) chloride. Herein, we report the coupling reactions of epoxides with allyl bromide in the presence of 1.1 equiv. of indium(I) chloride and a catalytic amount of palladium(0) catalyst to generate homoallyl alcohols. Mechanistic studies suggest that the products were formed *via* a cascade epoxide rearrangement–aldehyde allylation process.

The initial studies was carried out by treatment of styrene oxide and allyl bromide with indium(I) chloride in THF at ambient temperature in a Barbier-type manner in the presence of 5 mol% tetrakis(triphenylphosphine)palladium(0)[7] (Scheme 1). The allylation proceeded smoothly and gave 70% yield of the homoallylic alcohol after stirring overnight. Decreasing the amount of palladium catalyst to 2 mol% gave a similar result (67%), albeit the reaction took longer (24 h) to complete.



Scheme 1

Further efforts were then focused on searching better palladium catalysts to achieve better conversion and yield. Four homogeneous catalysts $Pd(PPh_3)_4$, $[Pd(allyl)Cl]_2$, $Pd(OAc)_2$ and $PdCl_2(PPh_3)_2$, and two heterogeneous mesoporous silica supported palladium(0) catalysts with pore diameter of 6 nm (NanoPd-6) and 2.6 nm (NanoPd-2.6) were used in these efforts. The heterogeneous catalysts were prepared by treatment of palladium acetate with diphenylphosphine ligands covalently bound on mesoporous silica supports. The silica supports were prepared by co-assembling surfactant with silicate species prepared by hydrolysis and condensation reactions[8] of tetraethoxysilane (TEOS, $Si(OCH_2CH_3)_4$) and propyldiphenylphosphinetriethoxysilane ($Ph_2PCH_2CH_2Si(OCH_2CH_3)_3$) in an acidic ethanol and water solution followed by selective removal of surfactant. Subsequent refluxing of the porous supports in a palladium acetate THF solution and reduction in H_2 atmosphere led to the formation of mesoporous supported catalysts with uniform pore diameter and surface area > 600 m^2 g^{-1}.[9] The immobilization of homogeneous catalysts *via* covalent attachment to a porous support is one of the possible ways to prepare well-defined and readily recyclable heterogeneous catalytic systems.[10]

The conversion and yield of the coupling reactions carried out in THF at ambient temperature for 24 h using these catalysts are summarized in Table 1. $Pd(PPh_3)_4$ exhibited the best conversion (82%) and yield (67%) among the homogenous palladium catalysts; whereas $[Pd(allyl)Cl]_2$, $Pd(OAc)_2$ and $PdCl_2(PPh_3)_2$ showed poor conversions (17%, 18% and 10% respectively) possibly due to their inefficient formation of π-allylpalladium(II) complexes. The heterogeneous catalysts have similar active sites but different pore sizes; interestingly, the catalyst with 6 nm pore diameter (NanoPd-6) showed better conversion (85%) and yield (74%) than the catalyst with 2.6 nm pore diameter (NanoPd-2.6) (conversion, 29%; yield, 15%). This suggests that the pore structure of the catalyst strongly affects the catalytic performance. The lower conversion and yield may be due to the slower rate of π-allylpalladium(II) formation within the narrow pore channels.

Subsequently, various epoxides were reacted with allyl bromide and indium(I) chloride by using the NanoPd-6 catalyst. Cyclic epoxides (Table 2, entries 6–8) and styrene oxide derivatives (Table 2, entries 1–5) including 2-methyl styrene oxide showed good yields of the target products. However, for acylic aliphatic epoxides (Table 2, entries 9–10), the use of either NanoPd-6 or $Pd(PPh_3)_4$ failed to give the target products.

Considering the high cost of palladium compounds, it is highly desirable to recover and reuse the palladium catalysts. In the present catalytic system, the heterogeneous palladium

Table 1 Palladium catalyst screening for coupling reaction of styrene oxide with allyl bromide[a]

Entry	Catalyst	Conversion[b] (yield)[c] (%)
1	$Pd(PPh_3)_4$	82 (67)
2	$[Pd(allyl)Cl]_2$	17
3	$Pd(OAc)_2$	18
3	$PdCl_2(PPh_3)_2$	10
4	NanoPd-6	85 (74)
6	NanoPd-2.6	29 (15)

[a] All reactions were carried out with 0.5 mmol styrene oxide, 1 mmol allyl bromide and 0.55 mmol indium(I) chloride in THF at room temp. for 24 h. [b] Determined by ^{1}H NMR of the crude product mixture. [c] Isolated yield after flash chromatography with hexane/EtOAc (20 : 1–15 : 1) eluents in parantheses.

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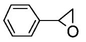
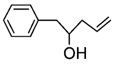
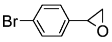
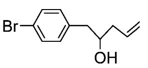
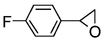
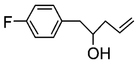
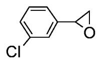
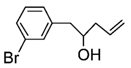
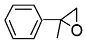
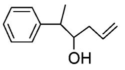
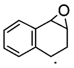
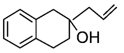
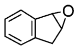
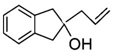
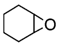
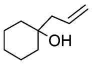
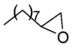
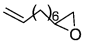
† Electronic supplementary information (ESI) available: experimental. See http://www.rsc.org/suppdata/cc/b3/b305161g/

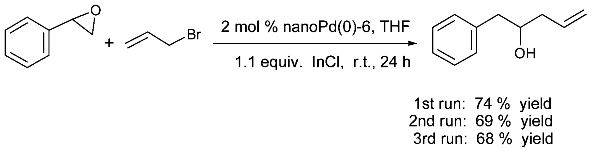
DOI: 10.1039/b305161g

Table 2 Allylation of various epoxides catalyzed by NanoPd-6

Entry	Epoxide		Products		Yield (%)[a]
1		**1a**		**2a**	74
2		**1b**		**2b**	62
3		**1c**		**2c**	76
4		**1d**		**2d**	69
5		**1e**		**2e**	58
6		**1f**		**2f**	71
7		**1g**		**2g**	83
8		**1h**		**2h**	47
9		**1i**	—		0
10		**1j**	—		0

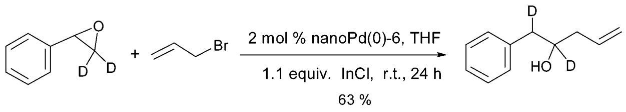
[a] Isolated yield after flash chromatography with hexane/EtOAc (20 : 1–15 : 1) eluents.

catalysts could be recovered and reused by simple filtration under nitrogen without significant loss of catalytic activity. It was shown that these heterogeneous catalysts could be reused three times and similar yields were obtained in each run (see Scheme 2).

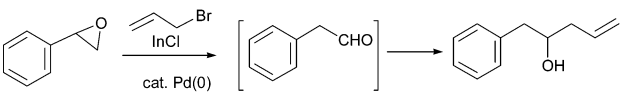


Scheme 2

In order to determine the mechanism of the product formation, 2,2-dideuteriostyrene oxide was reacted with allyl bromide under the standard conditions (Scheme 3). The reaction generated 1,2-dideuterio-1-phenyl-4-penten-2-ol in 63% yield, which suggests that the reaction proceeded *via* an epoxide rearrangement to give an aldehyde *in situ*, possibly catalyzed by In(III), followed by palladium-catalyzed addition of allylindium reagent to the aldehyde (Scheme 4).[6]



Scheme 3



Scheme 4

In conclusion, we have developed a novel InCl mediated coupling of epoxides with allyl bromide catalyzed by mesoporous silica supported palladium to give homoallyl alcohols. The heterogeneous catalyst can be readily recovered and reused without significant loss of its catalytic activity.

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Notes and references

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