

A new cascade for the one-pot synthesis of linear homoallylic alcohols with an allylic diindium reagent

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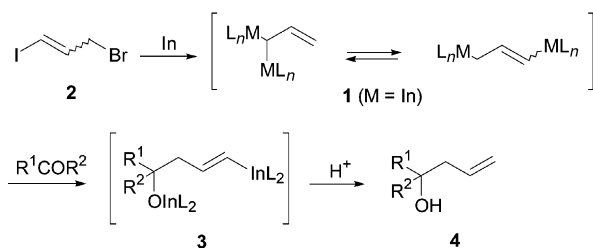
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A new cascade based on a novel allylic diindium reagent has been developed; the indium reagent prepared from 3-bromo-1-iodopropene successively coupled with carbonyl compounds and then with aryl, alkenyl or allyl halides in the presence of a Pd(0) catalyst to afford a convenient one-pot synthesis of linear homoallylic alcohols.

Organometallic compounds, which possess two metal-carbon bonds in one molecule, are synthetically attractive reagents; because, when they couple successively with two electrophiles, a three-component coupling can be achieved in one pot.¹ Although a number of organometallic reagents have hitherto been prepared and utilized, allylic dimetal compounds of type **1** are rare and only a few examples such as M = Li², Zn³ and Sn⁴ are known. Recently we described the preparation of the diindium reagent **1** (M = In) by oxidative addition of indium to 3-bromo-1-iodopropene (**2**).⁵ This reagent couples readily with carbonyl compounds leading to the corresponding homoallylic alcohols **4** via the vinylic indium compound **3** (Scheme 1). However, the reagent **3** could not be utilized for further transformations owing to the poor nucleophilicity of the vinylic indium-carbon bond. Now we have established a new cascade



Scheme 1

Table 1^a Tandem couplings of **1** (M = In) with benzaldehyde and iodobenzene

Entry	Solvent	Pd(PPh ₃) ₄ /mmol	T/°C	Yield of 5a (%)
1 ^b	DMA	0.03	rt	0 [72] ^c
2 ^b	DMA	0.05	110	18 (<i>E</i> : <i>Z</i> = 46:54)
3	DMA	0.03	rt	0 [68] ^c
4	DMA	0.03	110	56 (<i>E</i> only)
5	NMP	0.05	100	57 (<i>E</i> only)
6 ^d	NMP	0.03	100	34 (<i>E</i> only)
7	NMP	0.04 ^e	100	47 (<i>E</i> only)
8 ^f	NMP	0.10	100	67 (<i>E</i> : <i>Z</i> = 85:15)

^a Unless otherwise noted, reactions were carried out with **2** (1.0 mmol), PhCHO (0.50 mmol), PhI (1.0 mmol) and LiCl (3.0 mmol) in a solvent (6 mL) for 24 h. ^b Without LiCl. ^c Yield of 1-phenylbut-3-en-1-ol. ^d NaOEt was added in place of LiCl. ^e Pd₂(dba)₃ (0.02 mmol) and tris(2-furyl)phosphine (0.13 mmol) were used in place of Pd(PPh₃)₄. ^f With PhCHO (0.39 mmol).

based on **1** (M = In) involving allylation of carbonyls followed by Pd(0)-catalyzed coupling of the resulting vinylium with aryl, alkenyl or allyl halide, which provides a convenient one-pot synthesis of linear homoallylic alcohols.

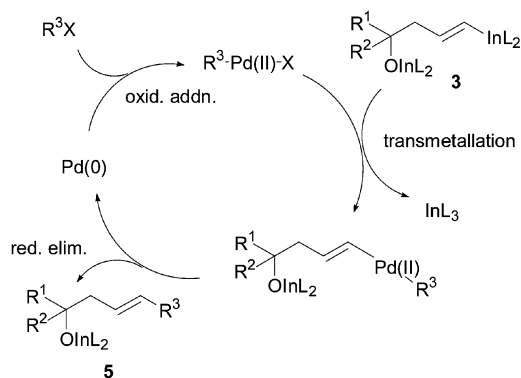
Iodobenzene and a catalytic amount of Pd(PPh₃)₄ were added to the vinylium reagent **3** prepared by the indium-mediated coupling of **2** with benzaldehyde at rt for 1 h. Although the addition of the second electrophile did not occur at rt (Table 1, Entry 1), the expected three-component coupling product **5a** was obtained in 18% yield at 110 °C with an *E*:*Z* ratio of 46:54 (Entry 2). The addition of LiCl resulted in the dramatic improvement both in the yield and *E*:*Z* selectivity: (*E*)-**5a** was obtained stereoselectively in 56% yield (Entry 4). The solvent NMP gave almost coincident results (Entry 5). The addition of NaOEt or the use of Pd₂(dba)₃-tris(2-furyl)phosphine in place of Pd(PPh₃)₄ also resulted in the selective formation of (*E*)-**5a** (Entries 6 and 7). The yield increased with increasing amounts of Pd(PPh₃)₄, though the *E*/*Z* selectivity was diminished (Entry 8).

The scope of this cascade was examined by changing the carbonyl compounds and the second electrophiles (Table 2).

Table 2^a Scope of the cascade reaction with **1** (M = In)

Entry	R ¹ COR ²	R ³ X	Yield (%) (<i>E</i> : <i>Z</i>)
1	CH ₃ (CH ₂) ₆ CHO	PhI	5b : 43 (100:0)
2	Ph-CHO	"	5c : 47 (100:0)
3	CH ₃ (CH ₂) ₅ COCH ₃	"	5d : 67 (70:30)
4	PhCOCH ₃	"	5e : 81 (59:41)
5	"	Ph-CH=CH ₂ -Br (<i>E</i> : <i>Z</i> =86:14)	5f : 50 (68:32)
6	"	CH ₂ =CH-CH ₂ -Cl	5g : 49 (76:24) ^b

^a Reactions were carried out in NMP by mixing **2** (1.0 mmol), indium (1.0 mmol) and a carbonyl compound (0.50 mmol) at rt for 1 h, and then the second electrophile (1.0 mmol) was reacted in the presence of Pd(PPh₃)₄ (0.10 mmol) and LiCl (3 mmol) at 100–110 °C for 24 h. ^b This *E*/*Z* assignment is tentative.



Scheme 2

Aliphatic and α,β -unsaturated aldehydes gave the corresponding three-component coupling products (Entries 1 and 2). The coupling with the aldehydes underwent with complete *E*-selectivity, though the yields were somewhat lower. Ketones also gave the linear homoallylic alcohols (Entries 3 and 4). As the second electrophiles, β -bromostyrene and allyl chloride were successfully used to give 1,3- and 1,4-dienes, respectively (Entries 5 and 6). The most plausible mechanism is depicted in Scheme 2. The vinylindium **3** undergoes transmetalation to a vinylpalladium(II) intermediate, which gives the three-component coupling products **5** by reductive elimination.

In contrast to the highly reactive nature of allylic indium reagents,⁶ the preparation and synthetic applications of vinylic indium compounds are strictly limited.⁷ The allylic diindium reagent **1** ($M = \text{In}$) possessing the two indium–carbon bonds of distinct reactivity can be prepared readily and can now be utilized for the tandem couplings with two electrophiles. The

success of the present cascade not only provides a new synthetic route for linear homoallylic alcohols, but also expands the scope of organoindium chemistry in organic synthesis by means of a combination with palladium catalysts.⁸

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