

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

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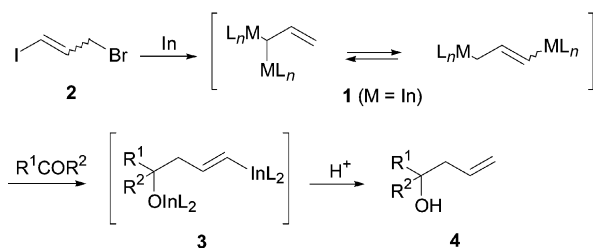
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A new cascade based on a novel allylic diindium reagent has been developed; the indium reagent prepared from 3-bromo-1-iodopropene successively coupled with carbonyl compounds and then with aryl, alkenyl or allyl halides in the presence of a Pd(0) 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.<sup>1</sup> 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 = Li<sup>2</sup>, Zn<sup>3</sup> and Sn<sup>4</sup> 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**).<sup>5</sup> 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<sup>a</sup> Tandem couplings of **1** (M = In) with benzaldehyde and iodobenzene

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

<sup>a</sup> 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. <sup>b</sup> Without LiCl. <sup>c</sup> Yield of 1-phenylbut-3-en-1-ol. <sup>d</sup> NaOEt was added in place of LiCl. <sup>e</sup> Pd<sub>2</sub>(dba)<sub>3</sub> (0.02 mmol) and tris(2-furyl)phosphine (0.13 mmol) were used in place of Pd(PPh<sub>3</sub>)<sub>4</sub>. <sup>f</sup> 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.

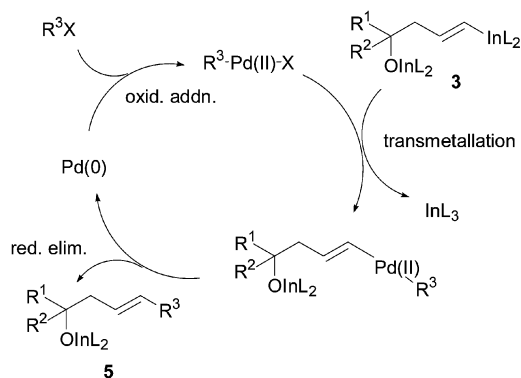
Iodobenzene and a catalytic amount of Pd(PPh<sub>3</sub>)<sub>4</sub> were added to the vinylium reagent **3** prepared by the indium-mediated coupling of **2** with benzaldehyde at rt for 1 h. Although the addition of the second electrophile did not occur at rt (Table 1, Entry 1), the expected three-component 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 Pd<sub>2</sub>(dba)<sub>3</sub>-tris(2-furyl)phosphine in place of Pd(PPh<sub>3</sub>)<sub>4</sub> also resulted in the selective formation of (*E*)-**5a** (Entries 6 and 7). The yield increased with increasing amounts of Pd(PPh<sub>3</sub>)<sub>4</sub>, 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<sup>a</sup> Scope of the cascade reaction with **1** (M = In)

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

<sup>a</sup> 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(PPh<sub>3</sub>)<sub>4</sub> (0.10 mmol) and LiCl (3 mmol) at 100–110 °C for 24 h. <sup>b</sup> This *E*/*Z* assignment is tentative.



Scheme 2

Aliphatic and  $\alpha,\beta$ -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,  $\beta$ -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,<sup>6</sup> the preparation and synthetic applications of vinylic indium compounds are strictly limited.<sup>7</sup> 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.<sup>8</sup>

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## Notes and references

- (a) I. Marek and L.-F. Normant, *Chem. Rev.*, 1996, **96**, 3241; (b) I. Marek, *Chem. Rev.*, 2000, **100**, 2887.
- (a) J. Vollhardt, H. J. Gais and K. L. Lukas, *Angew Chem., Int. Ed. Engl.*, 1985, **24**, 610; (b) H. J. Gais and J. Vollhardt, *Tetrahedron Lett.*, 1988, **29**, 1529.
- (a) J. F. Normant, J. C. Quirion, A. Alexakis and Y. Masuda, *Tetrahedron Lett.*, 1989, **30**, 3955; (b) L. Labaudinière, J. Hanaïzi and J. F. Normant, *J. Org. Chem.*, 1992, **57**, 6903; (c) J. F. Normant, *New J. Chem.*, 1990, **14**, 461; (d) L. Labaudinière and J. F. Normant, *Tetrahedron Lett.*, 1992, **33**, 6139.
- (a) D. Madec and J.-P. Férézou, *Tetrahedron Lett.*, 1997, **38**, 6657; (b) D. Madec and J.-P. Férézou, *Tetrahedron Lett.*, 1997, **38**, 6661.
- T. Hirashita, T. Kamei, T. Horie, H. Yamamura, M. Kawai and S. Araki, *J. Org. Chem.*, 1999, **64**, 172.
- (a) P. Cintas, *Synlett*, 1995, 1087; (b) J. A. Marshall, *Chemtracts-Organic Chemistry*, 1997, **10**, 481; (c) C.-J. Li and T.-H. Chan, *Tetrahedron*, 1999, **55**, 11 149; (d) B. C. Ranu, *Eur. J. Org. Chem.*, 2000, 2347.
- (a) I. Pérez, J. P. Sestelo and L. A. Sarandeses, *Org. Lett.*, 1999, **1**, 1267. Vinyliindium compounds prepared from allylindiation of alkynes were reported to couple with iodobenzene in the presence of Pd(0) catalyst. (b) N. Fujiwara and Y. Yamamoto, *J. Org. Chem.*, 1999, **64**, 4095.
- Recently, palladium-indium mediated Barbier-type allylations of carbonyls were reported. (a) J. A. Marshall and C. M. Grany, *J. Org. Chem.*, 1999, **64**, 8214; (b) U. Anwar, R. Grigg, M. Rasparini, V. Savic and V. Sridharan, *Chem. Commun.*, 2000, 645; (c) U. Anwar, R. Grigg and V. Sridharan, *Chem. Commun.*, 2000, 933; (d) S. Araki, T. Kamei, T. Hirashita, H. Yamamura and M. Kawai, *Org. Lett.*, 2000, **2**, 847.