Reaction of Allylic-type Diindium Compounds with Electrophiles

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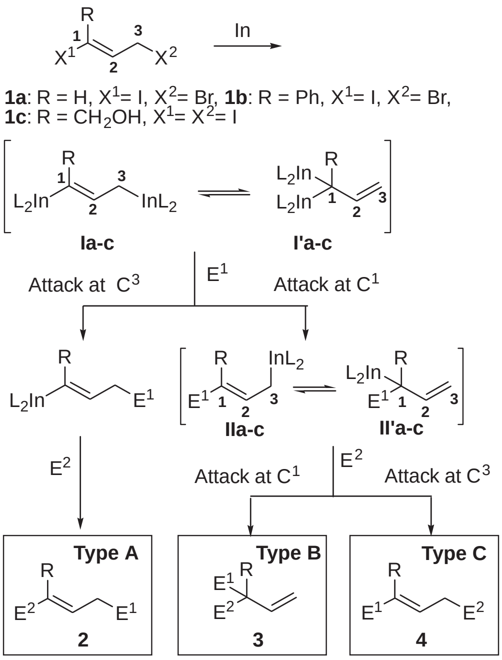
Allylic-type diindium reagents were prepared from 3-bromo-1-iodopropene (**1a**), 3-bromo-1-iodo-1-phenylpropene (**1b**), or 2,4-diiodobut-2-en-1-ol (**1c**) with metallic indium, and their successive coupling with electrophiles was examined. The coupling behavior of the diindium reagents was found to depend on the electrophiles and the substituent on the diindium compounds.

Organodimetallic compounds, which contain two metal–carbon bonds in one molecule, are attractive molecules from the standpoint of synthetic reagents.[1] We have reported that the oxidative addition of indium to 3-bromo-1-iodopropene (**1a**) generates diindiopropene **Ia** (**I′a**). This compound couples with carbonyl compounds and imines, and the resulting vinylindium compounds react further with aryl, alkenyl, or allyl halide in the presence of $Pd(PPh_3)_4$ to give linear homoallylic alcohols or amines.[2] The reaction courses of allylic-type diindium reagents with two electrophiles can be classified into three types, **A**–**C** (Scheme 1). We previously showed that the reaction of **Ia** (**I′a**) proceeds via type **A** course leading to **2**.[2]



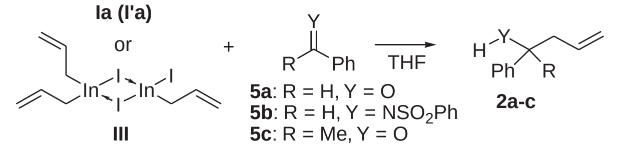
Type	nucleophilic attack first	second	product
A	C3	C1	**2**
B	C1	C1	**3**
C	C1	C3	**4**

Scheme 1. Reaction course of allylic-type diindium.

In order to estimate the difference in reactivity between diindiopropene **Ia** (**I′a**) and allylindium sesquiiodide (**III**) toward electrophiles, competitive reactions were performed by using benzaldehyde (**5a**), sulfonimine **5b**, and acetophenone (**5c**) as electrophiles (Table 1). It was found that the chemoselectivity of **Ia** (**I′a**) is higher than that of **III**. In the competitive reaction of **5a** and **5b**, allylindium **III** gave a mixture of **2a** and **2b**, whereas **2a** was selectively obtained with diindium **Ia** (**I′a**) (Entry 1, Table 1). The results of **5b**/**5c** indicate that diindiopropene **Ia** (**I′a**) reacts with **5b** approximately seven times faster than **5c**, but only twice as fast in the case of **III** (Entries 2 and 3).

Next, a diastereoselective allylation of imines **5d** derived from (*S*)-valine with **Ia** (**I′a**) and **III** was examined (Table 2). The reaction with **1a** afforded the allylated product with much higher selectivity (Table 2, Entry 1) than that with **III** (Entry 2). This reaction behavior of diindiopropene **Ia** (**I′a**) opens up a possibility for higher chemo- and stereoselective allylation than that with conventional allylindium reagent (**III**). Presumably, the difference between **I** and **III** may be explained by the Lewis acidity and/or the bulkiness arising from the two indium atoms on the diindiopropene.

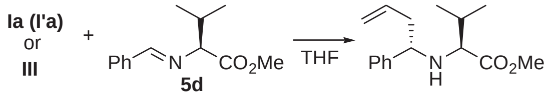
Table 1. Chemoselectivity of **Ia** (**I′a**) and **III** toward electrophiles[a]



Entry	Solvent	Ratio of Products/%[b] Diindiopropene **Ia** (**I′a**) **2a**	**2b**	**2c**	Allylindium sesquiiodide (**III**) **2a**	**2b**	**2c**
1	THF	100	0	—	63	37	—
2	THF	—	87	13	—	63	37
3	DMA	—	87	13	—	68	32

[a]All reactions were carried out with a half amount of the allylating agent to a 1:1 mixture of two electropliles (each 0.5 mmol) at room temperature for 17 h. [b]The ratio was determined on the basis of ^1H NMR analysis of a mixture of two products.

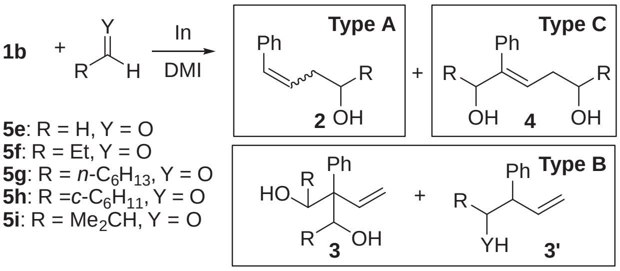
Table 2. Diastereoselective allylation of **5d** derived from (*S*)-valine



Entry	*Allylindium*	Conditions	Yield/%	*SS*:*RS*
1[a]	**Ia** (**I′a**)	rt, 44 h	54	98:2
2[b]	**III**	rt, 36 h	100	75:25

[a]The reaction was carried out with In (1.5 mmol), **1a** (0.75 mmol), and **5d** (0.50 mmol). [b]From Ref. 3.

Table 3. In-mediated reaction of **1b** with aldehydes and imine[a]



5e: R = H, Y = O
5f: R = Et, Y = O
5g: R = *n*-C_6H_{13}, Y = O
5h: R =*c*-C_6H_{11}, Y = O
5i: R = Me_2CH, Y = O

Entry	**5** (mol %)	**2** (%)	**3** (%)	**3′** (%)	**4** (%)
1	**5e** (200)	0	**3e**: 77	**3′e**: 23	0
2	**5f** (200)	0	**3f**: 15[b]	**3′f**: 5[b]	**4f**: 30[c]
3	**5g** (200)	0	0	**3′g**: 9[b]	**4g**: 30[b]
4	**5h** (200)	**2h**: 36[d]	0	**3′h**: 18[e]	0
5	**5i** (50)	**2i**: 44[f]	0	**3′i**: 42[b]	0
6	**5a** (50)	0	0	**3′a**: 77[e]	0
7	**5b** (50)	0	0	**3′b**: 90[g]	0

[a] All reactions were carried out with In (1.0 mmol), **1b** (0.50 mmol), and **5** in DMI (1,3-dimethyl-2-imidazolidinone, 1.5 mL) at room temperature for 4 h. [b] Diastereomeric ratio was not determined. [c] Two diastereomers (9:1) were found by ^{1}H and ^{13}C NMR. [d] E:Z = 40:60. [e] *Syn*:*anti* = <1:>99. [f] E:Z = 33:67. [g] *Syn*:*anti* = >99:<1.

To disclose further the reaction behavior of diindiopropene, new allylic-type diindium reagents bearing a phenyl (**1b**) or a hydroxymethyl group (**1c**) on the C^1 position were prepared. Prior to the reaction of **1b** with aldehydes, the existence of diindium **Ib** (**I′b**) was confirmed by the following reaction: A mixture of **1b** (0.50 mmol) and indium (1.0 mmol) in THF was stirred for 2 h. The reaction mixture was quenched with 1 M hydrochloric acid and the product was extracted with ether. The product was analyzed by GC, showing that allylbenzene was formed in 60% yield. This fact clearly indicates the formation of the diindium reagent **Ib** (**I′b**) and the protonolysis of **Ib** (**I′b**) proceeds via type **B** course.

Next, the diindium reagent **Ib** (**I′b**) was subjected to the reaction of aldehydes and it is found that the reaction courses are distinct depending on aldehydes (Table 3).

With formaldehyde (**5e**), diol **3e** was obtained in 77% yield together with **3′e** in 23% yield (Entry 1, Table 3). Propionaldehyde (**5f**) gave a regioisomer mixture of **3f** and **4f** along with a small amount of **3′f** (Entry 2). Hexanal (**5g**) gave diol **4g** and homoallylic alcohol **3′g** (Entry 3), whereas bulky aldehydes **5h** and **5i** gave no diol product but yielded homoallylic alcohols **2** and **3′** (Entries 4 and 5). With benzaldehyde (**5a**), homoallylic alcohol **3′a** was solely obtained in high yield with *anti*-selectivity (Entry 6), whereas sulfonimine **5b** gave **3′b** with *syn*-selectivity (Entry 7). As allylic indium compounds are known to be protonated at the γ-position, the *anti*- and *syn*-stereochemistry of **3′a** and **3′b** can be rationalized by the attack of the proton toward the resulting allylic indium compounds **IIb** from the less hindered direction with regio- and stereoselectivity (Figure 1).[4]

Finally, the reaction of **1c** with benzaldehyde was studied and the results are shown in Table 4. In DMI, diol **2′h** (type A) was obtained as a main product together with diol **3′h** (type B) and diene **6** (Entry 1, Table 4). In an aqueous medium, the yield of **6** was increased (Entry 2), whereas in THF **2′h** was obtained in 45% yield and **6** was scarcely observed (Entry 3). Diene **6** may come from the C^1 attack of benzaldehyde, followed by the elimination of $InOInL_2$ from **II′c** prior to protonolysis.

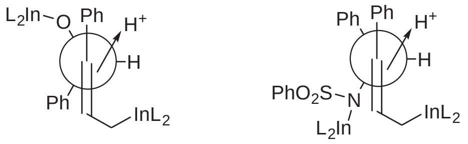
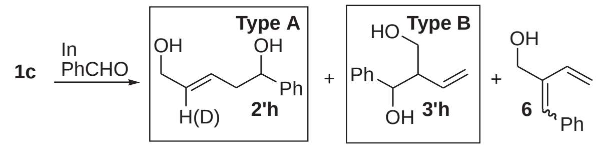


Figure 1.

Table 4. In-mediated reaction of **1c** with benzaldehyde[a]



Entry	Solvent	Yield/%		
		2′h (E:Z)	**3′h**	**6**
1	DMI	72 (30:70)	15	10[b]
2	THF–H_2O (1:1)	20 (80:20)	15	45[b]
3	THF	45 (50:50) (D 64%)[c]	22	trace

[a] All reactions were carried out with In (1.0 mmol), **1c** (0.50 mmol), and PhCHO (0.25 mmol) in solvent (1.0 mL) at room temperature for 2 h. [b] E:Z ratio was not determined. [c] Quenched by 1 M DCl.

In summary, the reaction behavior of the allylic-type diindium reagents toward electrophiles was found to differ considerably depending on both the electrophiles and the substituent on the diindiopropene. The coupling of **Ib** (**I′b**) proceeded via type **B** with small electrophiles, such as proton and formaldehyde, whereas the reaction course turned to type **A** and **C** with increasing the bulkiness of electrophiles. The diindiopropene **Ic** (**I′c**) bearing a hydroxymethyl group was prone to react with benzaldehyde via type **A** leading to the corresponding linear diol.

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References

1 a) I. Marek, L.-F. Normant, *Chem. Rev.* **1996**, *96*, 3241. b) E. M. Flamme, W. R. Roush, *J. Am. Chem. Soc.* **2002**, *124*, 13644.

2 a) T. Hirashita, H. Yamamura, M. Kawai, S. Araki, *Chem. Commun.* **2001**, 387. b) T. Hirashita, Y. Hayashi, K. Mitsui, S. Araki, *J. Org. Chem.* **2003**, *68*, 1309.

3 T. Basile, A. Bocoum, D. Savoia, A. Umani-Ronchi, *J. Org. Chem.* **1994**, *59*, 7766.

4 M. N. Paddon-Row, N. G. Rondan, K. N. Houk, *J. Am. Chem. Soc.* **1982**, *104*, 7162.