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Allylation of epoxides with allylic indium reagents

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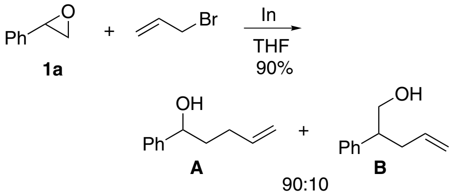
Abstract—Allylindium sesquihalide reacts with epoxide to give homoallyl alcohol via a 1,2-shift reaction. In contrast, allylindate gives the ring-opening product without rearrangement.

1. Introduction

Epoxides are valuable synthetic units that are used for α-functionalized alcohols by nucleophilic attack with a *trans*-stereospecific ring-opening and Lewis acid-catalyzed rearrangements to the corresponding carbonyl compounds.[1] The reaction of organometallic compounds with epoxides gives 1,2-addition products and/or rearrangement products depending on the nature of the organometallics.[2] Allylindium reagents have received much attention in the past decade[3] and the reaction with epoxide was first examined by Yadav et al., who reported that the reaction of allyl bromide with styrene oxide (**1a**) in the presence of indium in THF gave the corresponding ring-opening alcohols **A** and **B** in high yield (Scheme 1).[4]

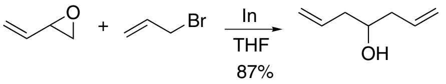
Recently, Oh et al., reported that the reaction of terminal vinyl epoxides with allylindium sesquibromide gave various bis(homoallyl) alcohols via a consecutive 1,2-shift reaction (Scheme 2).[5]



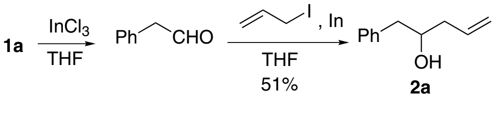
Scheme 1.

The difference in the above reactions was rationalized by the nature of the epoxides employed. However, the assignment of the structure of **A** on the basis of the ^{1}H NMR data seem to be questionable; the resonance at δ 2.75 ppm of **A** was assigned as the protons of the α-carbon. It is more reasonable for the signal to be assigned as the benzyl protons in 1-phenylpent-4-en-2-ol (**2a**). Alcohol **2a** was easily obtained without ambiguity by the allylation of phenylacetaldehyde, which is known to be easily available by the reaction of epoxide **1a** with $InCl_3$ (Scheme 3).[6] The allylation of this aldehyde with allylindium sesquiiodide gave **2a** in 51% yield and the ^{1}H NMR data of **2a** is coincident with the reported data as **A**.

Now, we disclose here the results of the reactions of epoxides with various types of allylindium reagents, which reveal that the reaction highly depends both on the epoxides and the allylic indium reagents.



Scheme 2.



Scheme 3.

Keywords: Indium; Ate complex; Epoxide; Allylation.

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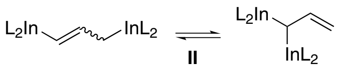
2. Results and discussion

The reaction of **1a** with allylindium sesquiiodide (**I**) was first conducted as follows: allyl iodide (1.5 mmol) and indium (1.0 mmol) were mixed in dry THF (2 mL) at room temperature for 1 h. To the resulting **I**, **1a** (1.0 mmol) was added and the mixture was stirred for 3 h. The reaction was quenched with 1 M hydrochloric acid and the product was extracted with ether. The crude product was purified by column chromatography on silica gel (EtOAc–hexane = 1:9) to give **2a** in 75% yield (Table 1, entry 1).[7] These results show that allylindium sesquihalide has enough Lewis acidity to rearrange epoxides to aldehydes as $InCl_3$ and that the reaction of epoxides with allylindium sesquihalide proceeds via transformation of the epoxides to the corresponding aldehydes as in the case of vinyl epoxides. Next, the reactions of other allylic indium reagents with epoxides were examined. The reaction of the allylic-type diindium reagent **II**, prepared from 3-bromo-1-iodopropene and indium,[8] with **1a** selectively gave **2a** in good yield (entry 2). No coupling product incorporated with two molecules of **1a** was found.



Tetraorganoindium ate-complex (indate) is postulated as a strong Lewis base and its reaction with epoxides is considered to be distinct from that of allylindium sesquihalide.[9] As expected, allylindate **III**, prepared from **I** with MeLi, underwent ring-opening reaction to give a mixture of alcohols **3a** and **4a** in 76% yield as shown in Scheme 4 (entry 3).[10]

The reaction of **I** with 2-styryloxirane (**1b**) gave the corresponding homoallylic alcohol **2b** in good yield via the rearrangement to the aldehyde (entry 4), whereas allylindate **III** reacted with epoxide **1b** at the substituted carbon to give **3b** together with a small amount of the 1,4-addition product **5** (entry 5). Allylindate **IV**, generated from $InCl_3$/allylmagnesium bromide/MeLi = 1:1:3, showed the same tendency and afforded **3b** selectively (entry 6). The rearrangement product **2b** was obtained in entry 6 as a by-product, which may be caused by the presence of magnesium salt. The reaction of alkyl epoxide **1c** resisted allylation, and heating and prolonging the reaction time were needed for allylation to furnish **2c** in low yield (entry 7). On the contrary, the reaction of allylindate **III** proceeded smoothly via nucleophilic attack at the less hindered carbon to give **4c** in high yield (entry 8). In the reactions involving allylmethylindates, (entries 3, 5, 6 and 8) the allyl group was selectively migrated to epoxide as the reaction with allylic halides in our previous report.[9]

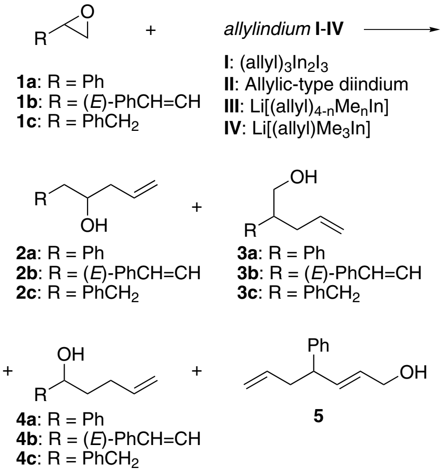
Table 1. Reaction of epoxides with allylindium reagents[a]

Entry	1	Allylindium	Conditions	Total yield (%) **2**:**3**:**4**
1	**1a**	**I**	THF, rt, 3 h	75 (100:0:0)
2	**1a**	**II**	THF, 3 h	65 (100:0:0)
3	**1a**	**III**	$THF–Et_2O$ (4:5), rt, 1 h	76 (0:38:62)
4	**1b**	**I**	THF, rt, overnight	57 (100:0:0)
5	**1b**	**III**	$THF–Et_2O$ (4:5) rt, 0.5 h	70 (0:100:0)[b]
6	**1b**	**IV**	$THF–Et_2O$ (4:5), rt, 1 h	80 (19:81:0)[c]
7	**1c**	**I**	THF, rfx, overnight	26 (100:0:0)
8	**1c**	**III**	THF, rt, 2 h	86 (0:0:100)

[a] All reactions were performed with allylindium/epoxide = 1:1.

[b] The 1,4-adduct **5** was obtained in 2% yield.

[c] The 1,4-adduct **5** was obtained in 5% yield.



Scheme 4.

In general, strong nucleophiles attack at the least hindered carbon of epoxide due to steric effect.[2] Allylindate favoured the attack at the less hindered carbon of alkyl epoxide **1c**. However, the regioselectivity is not a simple issue. The coordination of the counter ion to the oxygen of epoxide causes polarization between the C–O bond and a positive charge is developed at the ring carbon, where the ability to stabilize the positive charge is one reason to determine the regioselective attack of nucleophiles. Indeed, the attack at the substituted (benzyl) carbon of **1a** occurred to some extent (entry 3). The same tendency was observed in the case of allylmanganate.[2] When vinyl epoxide **1b** was employed, the 1,2-addition competes with the 1,4-additon. The 1,2-adducts coupled at the allylic carbon were much favoured although a small amount of the 1,4-adduct **5** was obtained (entries 5 and 6). The observed ratio 1,2-/1,4-adduct is similar to that with butylaluminate.[2e]

In summary, we have demonstrated that allylindium sesquihalide has enough Lewis acidity to induce the rearrangement of epoxide prior to the direct allylation, and the resulting aldehydes undergo allylation to give the corresponding homoallylic alcohols irrespective of the substituent of epoxides. In contrast, allylindate directly reacts with epoxides to give the ring-opening products. The regioselectivity of the allylation is dependent on the substituent of epoxides.

Acknowledgements

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