# *Communications to the Editor*

## Regio- and Stereoselective Allylindation of Allenols Regulated by a Hydroxyl-Chelated Bicyclic Transition State

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Carbometalation of unsaturated compounds is one of the most important procedures in organometallic chemistry from both theoretical and practical standpoints.[1] A variety of unsaturated substrates such as alkenes and alkynes have hitherto been employed; however, allenes and their derivatives have received relatively little attention.[2] We have recently demonstrated that allylic indium sesquihalides react, stereoselectively but not regioselectively, with terminal alkynols to give allylindation products.[3] In this reaction, it was shown that the presence of a neighboring hydroxyl group is essential for smooth allylindation; the hydroxyl group, without formation of the indium alkoxide, coordinates to indium and facilitates the allylation of alkynols. In order to examine the generality of this acceleration and selectivity control based on the hydroxyl chelation, we have undertaken allylindation of several hydroxyl-containing alkenes and alkynes and found that allylindation of allenols with allylic indium sesquihalides proceeds, unlike the alkynol cases, with excellent regio- and stereoselectivity to give (*E*)-2,6-heptadien-1-ol derivatives in high yields.

**Scheme 1**

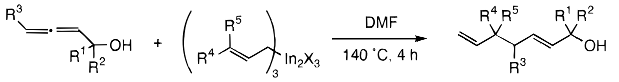
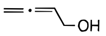
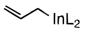
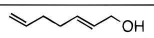
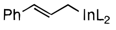
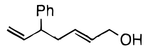
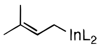
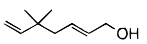
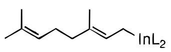
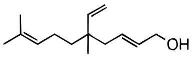
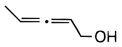
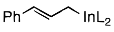
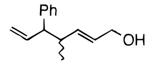
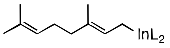
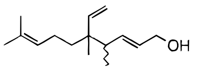
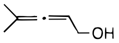
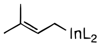
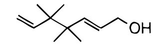
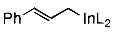
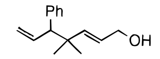
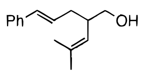
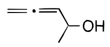
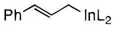
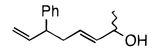
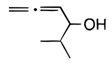
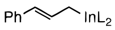
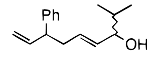
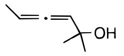
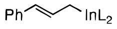
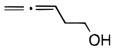
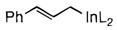
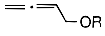
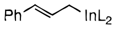


**Table 1.** Allylindation of Allenols[a]

| Entry | Allenol | Allylindium | Product(s) | Yield (%)[b] |
|---|---|---|---|---|
| 1 |  |  |  | 44 (100)[c] |
| 2 | |  |  | 97 |
| 3 | |  |  | 79 |
| 4 | |  |  | 89 |
| 5 |  |  |  | 99<br>(72:28) |
| 6 | |  |  | 78<br>(65:35) |
| 7 |  |  |  | 17 |
| 8 | |  | <br> | 54<br>(61:39)[d] |
| 9 |  |  |  | 44<br>(67:33) |
| 10 |  |  |  | 63<br>(61:39) |
| 11 |  |  | no reaction | |
| 12 |  |  | no reaction | |
| 13 | <br>R=Me,CH₂Ph |  | no reaction | |

[a] All reactions were done with allenol (1 mmol) and allylindium sesquihalide (0.5 mmol) in DMF (3 mL) at 140 °C for 4 h. [b] Isolated yield. Unless otherwise noted, numbers in parentheses refer to diastereomeric ratio. [c] Glc yield. [d] Ratio of the products.

The allylindation of allenols was conducted in DMF at about 140 °C for 4 h (Scheme 1).[4] Results are summarized in Table 1. Allylindium sesquiiodide allylated selectively the terminal carbon of 2,3-butadien-1-ol yielding 2,6-heptadien-1-ol quantitatively (entry 1). The stereochemistry of the double bond was determined to be *E*, by the IR spectrum and comparison with an authentic sample,[5] implying that the indium reagent added from the face of allene *syn* to the hydroxymethyl group. No other regio- and stereoisomers were detected in the reaction mixture. With $\gamma$-substituted allylic indium sesquibromides, the coupling occurred selectively at the $\gamma$-carbon (entries 2−4). Substituents at the $C^4$-carbon of allenol showed no significant effects on the reaction (entries 5 and 6), though a combination of the $\gamma,\gamma$-disubstituted allylindium reagent with the 4,4-disubstituted allenol gave a considerably lower yield owing to severe steric repulsion (entry 7). With these substituted allenols, the diastereoselectivity was unfortunately only modest. The reaction of 4-methyl-2,3-pentadien-1-ol and cinnamylindium (entry 8) gave two isomeric products, of which the homoallyl alcohol was confirmed to be derived from the initially produced allylic alcohol via a [3.3]-sigmatropic rearrangement under the reaction conditions. Substituents on the $C^1$-carbon, on the other hand, significantly affected the reaction. Secondary allenols showed diminished reactivity (entries 9 and 10), and the tertiary allenol did not react at all owing to the steric crowding around the hydroxyl group (entry 11). In sharp contrast to the smooth reactions of 2,3-butadien-1-ol, 3,4-pentadien-1-ol did not give any allylindation products under similar reaction conditions (entry 12). The importance of a neighboring hydroxyl group for smooth allylindation was also demonstrated by the fact that the protection of the hydroxyl group of 2,3-butadien-1-ol as a methoxy or benzoxy group completely inhibited the allylindation

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(1) For recent reviews on carbometalation, see: (a) Knochel, P. Carbometallation of Alkenes and Alkynes. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, pp 865−911. (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38−52. (c) Norman, J. F.; Alexakis, A. *Synthesis* **1981**, 841−870.

(2) Examples of carbometalation of allenes. Allylzincation (allylcupration): Norman, J. F.; Quirion, J. Ch.; Masuda, Y.; Alexakis, A. *Tetrahedron Lett.* **1990**, *31*, 2879−2882. Norman, J. F.; Quirion, J. Ch.; Alexakis, A.; Masuda, Y. *Tetrahedron Lett.* **1989**, *30*, 3955−3958. Norman, J. F.; Quirion, J. Ch. *Tetrahedron Lett.* **1989**, *30*, 3959−3962. Allylmagnesiation: Richey, H. G., Jr.; Szucs, S. S. *Tetrahedron Lett.* **1971**, 3785−3787. Allylboration: Mikhailov, B. M. *Pure Appl. Chem.* **1974**, *39*, 505−523 and references cited therein.

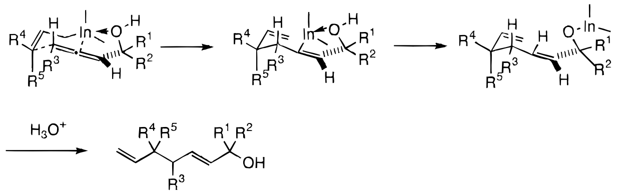
(3) Araki, S.; Imai, A.; Shimizu, K.; Yamada, M.; Mori, A.; Butsugan, Y. *J. Org. Chem.* **1995**, *60*, 1841−1847.

(4) The following reaction of 2,3-butadien-1-ol with cinnamylindium represents a general procedure: to a solution of cinnamylindium sesquibromide, prepared according to the published method[9] from indium powder (1.0 mmol) and cinnamyl bromide (1.5 mmol) in DMF (3 mL), was added 2,3-butadien-1-ol (1.0 mmol), and the mixture was heated at 140 °C for 4 h. The reaction was quenched by the addition of diluted hydrochloric acid, and the product was extracted with ether. The extracts were washed with brine and dried ($Na_2SO_4$). The solvent was removed, and the residue was distilled with a Kugelrohr apparatus (bath temperature: 105 °C/3 Torr) to give 5-phenyl-2,6-heptadien-1-ol (97%).

(5) Fukuzawa, S.; Sakai, S. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3308−3314.

S0002-7863(95)04318-6 CCC: $12.00

**Scheme 2**



(entry 13).[6] When tributylindium was used in place of allylic indium reagents, no carbometalation occurred.

The high regio- and stereoselectivity observed in this allenol allylation as well as the marked acceleration by a neighboring hydroxyl group can be best interpreted in terms of a hydroxyl-chelated bicyclic transition state (Scheme 2). The hydroxyl group is considered to coordinate to the indium atom forming a chelated five-membered ring; this extrudes the allylic $\gamma$-terminus to allenol C$^4$-carbon, consequently forming a bicyclic transition state. High regio- and stereoselectivity are realized through this transition state, and the resulting vinylindium compound could be spontaneously protonated by the hydroxyl proton to furnish the (*E*)-allylic alcohol indium salt. It is interesting to compare the high regioselectivity of the present allylindation of allenols with that of the previously reported alkynols.[1] The latter generally gave mixtures of two isomeric dienols arising from both "intra-" and "intermolecular" allylindation, whereas allylindation of allenols proceeds exclusively in the intramolecular fashion to afford high regioselectivity. The low reactivity of 3,4-pentadien-1-ol (entry 12) could be explained in terms of a hydroxyl-chelated six-membered ring in the transition state, which must be energetically less favorable compared with the corresponding five-membered ring.[7] With respect to the low diastereoselectivities in entries 5 and 6, it is possible that the indium-containing chairlike arrangement might be distorted owing to the large atomic radius of indium metal; accordingly, the energy difference is small between the two transition states, in which the R$^3$ group of allenol adopts an equatorial or axial position.[8] Similarly, the low diastereoselectivities in entries 9 and 10 suggest that the stereochemical course is little affected by the configuration of the substituent (R$^1$ or R$^2$) on the allenol C$^1$-carbon. Attempts to improve the diastereoselectivity, by changing the solvent and reaction temperature, were unsuccessful.

In summary, allylindation of allenols by allylic indium sesquihalides has been found to proceed with high regio- and stereoselectivity via a hydroxyl-chelated bicyclic transition state. It has also been demonstrated that allenols are useful in organic synthesis in combination with the unique nature of allylic indium reagents.

**Acknowledgment.** This work was supported by a Grant-in-Aid for Scientific Research (No. 07651030) from the Ministry of Education, Science and Culture, Japan.

**Supporting Information Available:** Spectroscopic and analytical data for the products in Table 1 (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA954318G

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[6] The importance of a free hydroxyl group was also demonstrated in indium-prompted allylation of α-hydroxy aldehydes: Paquette, L. A.; Mitzel, T. M. *Tetrahedron Lett.* **1995**, *36*, 6863−6866.

[7] 4-Pentyn-1-ol, which should form a similar chelated six-membered ring, is reported to be inert to allylindation.[3]

[8] Similarly, poor diastereoselectivity was observed in the allylation of carbonyl compounds with allylic indium sesquihalides: Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831−1833.

[9] Araki, S.; Shimizu, T.; Johar, P. S.; Jin, S.-J.; Butsugan, Y. *J. Org. Chem.* **1991**, *56*, 2538−2542.