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# Preparation and Reactions of Allenic Zirconium Species from Propargylic Ether Derivatives

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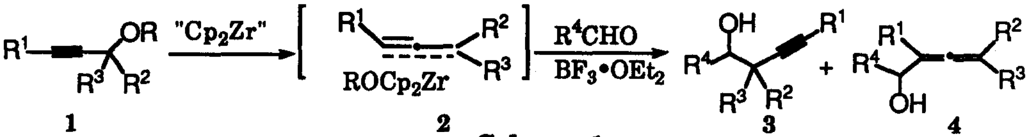
*Key Words:* zirconocene; zirconacyclopropene; propargylic ether derivatives; allenic zirconium species

***Abstract:*** *The generation of allenic zirconium intermediates by treating propargylic ether derivatives with "$Cp_2Zr$" and their reactions with aldehydes in the presence of borontrifluoride etherate yield anti-β-acetylenic alcohols along with α-allenic alcohols.*

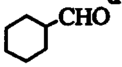
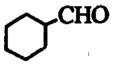
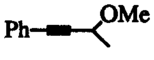
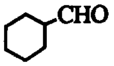
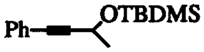
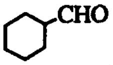
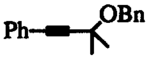
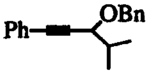
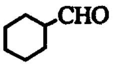
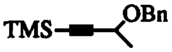
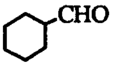
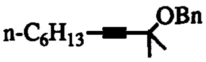
The reactions of low valent zirconium species with unsaturated compounds have been widely studied for the formation of carbon-carbon bonds in organic synthesis.[1] In our recent study on zirconium chemistry,[2] a method for preparing allylic zirconium species was established via elimination of the alkoxy group of α-alkoxy zirconacyclopropane derivatives, obtainable *in situ* from allylic ethers with putative zirconocene "$Cp_2Zr$" (Cp = cyclopentadienyl).[3] The allenic zirconium species **2**, a very important reactive species in organic synthesis,[4] could be similarly obtained from propargylic ethers. This paper reports the preparation of **2** from propargylic ethers **1** with "$Cp_2Zr$" and stereo- and regioselective reactions with aldehydes in the presence of borontrifluoride etherate ($BF_3$•$OEt_2$).[5] The ratio of the β-acetylenic and α-allenic alcohols (**3** and **4**) obtained from the reaction of **2** with aldehyde appeared to depend on the substitution pattern of the substrate, bulkiness of the substituent ($R^2$ or $R^3$) and the reacting aldehyde. It is also shown that the anti/syn ratio of **3** was greatly influenced by the reacting aldehyde.



**Scheme 1**

The results of reactions of **2** with aldehydes are shown in Table I. In all cases, generation of the reactive zirconium species **2** was clearly shown to proceed without the recovery of any of the starting propargylic ethers.[6] In subsequent reactions of the intermediately generated **2** with aldehydes, $BF_3$•$OEt_2$ was necessary for obtaining good yields of the products (see, entries 1 and 3). Although poor diastereoselectivities in the reactions of **2** with benzaldehyde were observed,[7] the reaction with cyclohexanecarboxaldehyde showed the excellent regio- and anti-diastereoselectivity in the formation of **3** (entry 4). These results are in remarkable contrast to the formation of syn-β-acetylenic alcohols in the case of allenylstannanes.[5]

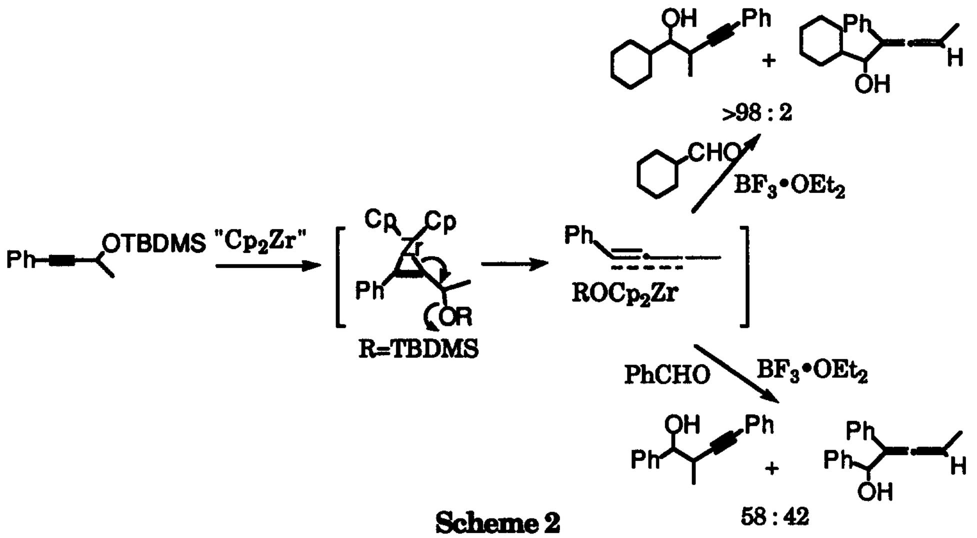
**Table I. Reactions of 2 with Aldehydes in the Presence of $BF_3 \cdot OEt_2$**

| Entry | Substrate | Aldehyde | 3 : 4 | anti-3 : syn-3[a,b] | Yield (%)[c] |
|---|---|---|---|---|---|
| 1 |  | PhCHO[d,e] | 79 : 21 | 3 : 1 | 19[f] |
| 2 | | PhCHO | 86 : 14 | 3 : 1 | 80 |
| 3 | |  [d,e] | 97 : 3 | 31 : 1 | 23[f] |
| 4 | |  | 94 : 6 | >49 : 1[g] | 76 |
| 5 |  |  | 95 : 5 | 29 : 1 | 65 |
| 6 |  | PhCHO | 58 : 42 | 3 : 1 | 49[f] |
| 7 | | PhCHO | 44 : 56[h] | 3 : 1 | 42[f] |
| 8 | |  | >98 : 2[g,h] | 22 : 1 | 73[f] |
| 9 |  | PhCHO[e] | >98 : 2[g,h] | -------- | 51[f] |
| 10 |  | PhCHO | 98 : 2 | 3 : 1 | 89 |
| 11 | |  | >98 : 2[g] | 49 : 1 | 86 |
| 12 |  | PhCHO | 80 : 20 | 2 : 1 | 49 |
| 13 | |  | 78 : 22 | 5 : 1 | 49 |
| 14 |  | PhCHO[e] | >98 : 2[g,h] | -------- | 68 |

a) Regio- and diastereoisomeric ratios were determined by 400MHz $^1H$-NMR spectroscopy. b) The anti/syn ratio was determined for 3. The isomeric ratio of 4 was not determined. The relative stereochemistry of 3 was determined as shown in ref. 8. c) Isolated yields of a mixture of regio- and diastereoisomers. d) $BF_3 \cdot OEt_2$ was not used. e) Reactions of 2 with aldehydes were carried out at 50°C overnight. f) Significant amounts (10-40%) of allene derivatives derived from protonation of 2 were obtained. g) No minor isomer could be detected by 400MHz $^1H$-NMR spectrum. h) The *in situ* generated 2 was heated at 50°C overnight.

Typical experimental procedure is as follows. Under an argon atmosphere, to a solution of zirconocene dichloride (210mg, 0.72mmol) in THF (3ml) was added a solution of n-butyllithium (2eq) at -78°C. After being stirred at -78°C for 1hr, a solution of **1** (0.6mmol) in THF (2ml) was added and the reaction temperature was raised to ambient temperature. The resultant mixture was stirred at the same temperature for 3hr. A solution of aldehyde (0.9mmol) and $BF_3 \cdot OEt_2$ (136mg, 0.96mmol) in THF (2ml) was then added dropwise to the reaction mixture at 0°C and resultant solution was stirred at ambient temperature overnight. After quenching the reaction mixture by 10% HCl, the mixture was extracted with ether. The usual work up and purification by column chromatography on silica gel gave mixed products of regio- and diastereoisomers.

In the reaction of **1** ($R$=TBDMS, $R^1$=Ph, $R^2$=H, $R^3$=$CH_3$) with benzaldehyde in the presence of $BF_3 \cdot OEt_2$, a formation of significant amount of α-allenic alcohol and a slight changing of the ratio of regioisomers upon heating of the *in situ* generated **2** at 50°C were observed (entries 6, 7). When cyclohexanecarboxaldehyde was used, β-acetylenic alcohol was obtained as the sole regioisomer (entry 8). Unlike the addition of benzaldehyde, heating of the reactive zirconium species **2** at 50°C overnight, followed by addition of cyclohexanecarboxaldehyde did not change the product ratio (α-allenic/β-acetylenic alcohol). It is known that β-acetylenic alcohols are the major products obtained from allenic organometallics and aldehydes through SEi' or SE2' process. Indeed, zirconium intermediate **2** derived from **1** ($R$=Bn, $R_1$=Ph, $R_2$=H, $R_3$=$CH_3$) with "$Cp_2Zr$" showed the strong IR absorption at 1900 $cm^{-1}$ corresponding to allenic zirconium species.[4b,7] Although the presence of allenic zirconium intermediate was established, the precise reaction mechanism for the addition of the reactive zirconium species **2** to aldehyde in the presence of $BF_3 \cdot OEt_2$ is unclear.



**Scheme 2**

In conclusion, we have developed a new method for preparing the allenic zirconium species via β-elimination of alkoxy group on α-alkoxy zirconacyclopropene, which can be easily prepared from chemically stable propargylic ethers and "$Cp_2Zr$". The reactions of *in situ* generated allenic zirconium species with aldehydes in the presence of $BF_3 \cdot OEt_2$ yielded anti-β-acetylenic alcohol as the major isomer.

## References and Notes

1) For reviews, see: a) Buchwald, S. L.; Nielsen, R. B. *Chem. Rev.*, **1988**, *88*, 1047-1058. b) Negishi, E.; Takahashi, T. *Synthesis*, **1988**, 1-19. c) Buchwald, S. L.; Fisher, R. A. *Chemica Scripta*, **1989**, *29*, 417-421. d) Negishi, E. *Chemica Scripta*, **1989**, *29*, 457-468 and references cited therein.

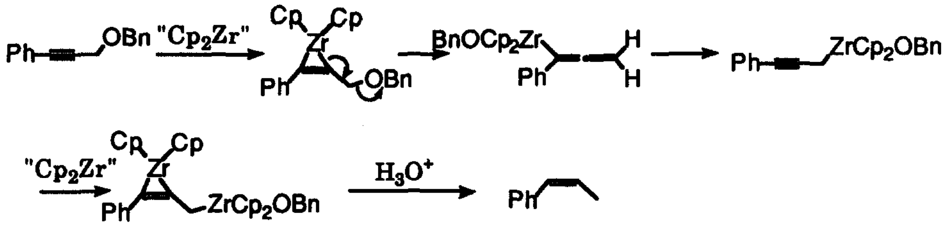
2) Ito, H.; Taguchi, T.; Hanzawa, Y. *Tetrahedron Lett.*, in press.

3) This preparative method of "$Cp_2Zr$" was first applied to organic synthesis by Negishi et al.: a) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.*, **1986**, *27*, 2829-2832. See also: b) Swanson, D. R.; Negishi, E. *Organometallics*, **1991**, *10*, 825-826 and references cited therein.

4) For reviews on the addition reactions of allenic metals to carbonyl compounds, see: a) Klein, J. Propargylic metalation. In *The chemistry of the carbon-carbon triple bond*; Patai, S., Ed.; John Wiley and Sons, Inc.: New York, 1987; pp. 343-379. b) Moleau, J. -L. Organometallic derivatives of allenes and ketenes. In *The chemistry of ketenes, allenes and related compounds*; Patai, S., Ed.; John Wiley and Sons, Inc.: New York, 1980; pp. 363-413. See also: c) Furuta, K.; Ishiguro, M.; Haruta, R.; Ikeda, N.; Yamamoto, H. *Bull. Chem. Soc. Jpn.*, **1984**, *57*, 2768-2776 and references cited therein.

5) The reactions of allenylstannanes with aldehydes in the presence of $BF_3 \cdot OEt_2$ gave syn-β-acetylenic alcohols as a major product; a) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.*, **1990**, *55*, 6246-6248. b) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.*, **1991**, *56*, 3211-3213.

6) In the reaction of **1** (R=Bn, $R^1$=Ph, $R^2$=$R^3$=H) with equimolar amount of "$Cp_2Zr$", the recovery of starting material along with a formation of (Z)-β-methylstyrene was observed by quenching of the reaction mixture with 10% HCl. This observation is considered to be a result of the very rapid formation of zirconacyclopropene **5** by the reaction of second "$Cp_2Zr$" with propargylic zirconium intermediate (*vide infra*). When two equimolar amount of "$Cp_2Zr$" was employed, no trace of starting material was recovered.



**5**

7) In the case of allenyltitaniums, the similar results have been reported; Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Org Chem.*, **1982**, *47*, 2225-2227.

8) The stereochemistries of the products in entries 1, 2, 6, 7 ($R^1$=Ph, $R^2$=Me, $R^3$=H, $R^4$=Ph) were determined by comparison of spectral data with authentic sample obtained by opening reaction of the corresponding epoxide according to the reported procedure, see: Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.*, **1983**, *24*, 391-394. The stereochemistries of the products in entries 3, 4, 5, 8 ($R^1$=Ph, $R^2$=Me, $R^3$=H, $R^4$=cy-$C_6$) and 12, 13 ($R^1$=TMS, $R^2$=Me, $R^3$=H, $R^4$=Ph or cy-$C_6$) were determined by comparison of spectral data with authentic samples, see: ref. 4c. The stereochemistry of the product in entry 10 ($R^1$=Ph, $R^2$=iso-Pr, $R^3$=H, $R^4$=Ph) was determined by comparison of spectral data of β-hydroxy-α-isopropylbenzenepropanoic acid methyl ester derived from the major product of entry 10 with authentic sample, see: Ayi, A. I.; Remli, M.; Guedj, R. *J. Fluorine Chem.*, **1981**, *17*, 127-143. The stereochemistry of entry 11 ($R^1$=Ph, $R^2$=iso-Pr, $R^3$=H, $R^4$=cy-$C_6$) was speculated in analogy with entry 10.

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