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# Synthesis of allenylzinc reagents by 1,2-rearrangement of alkynyl(disilyl)zincates derived from acetylenic epoxides and acetylenic aziridines



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## ABSTRACT

Lithium alkynyl(disilyl)zincates obtained from metalated ethynylloxiranes, as well as from *N*-*tert*-butanesulfinyl(ethynyl)aziridines or *N*-*tert*-butanesulfonyl(ethynyl)aziridines, undergo 1,2-migration of the organosilyl group with ring opening of the oxirane or aziridine ring by  $S_N1$  displacement. A developed protocol that involves *n*BuLi for the metalation step offers a straightforward approach to the corresponding  $\delta$ -oxy- and  $\delta$ -amino  $\alpha$ -silyl allenylzinc intermediates. The reagents derived from the epoxides are amenable to subsequent in situ condensation with aldehydes or ketones to provide 1,3-diols but not those derived from aziridines that only react sluggishly in similar condensations.

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## 1. Introduction

Allenylmetal reagents [1], including allenylzincs [2], are versatile organometallic species that have been used intensively in organic synthesis. For more than a decade, work from our laboratories [3] and others [1,2] have demonstrated that  $\alpha$ -silyl-substituted allenylzincs are a particularly useful substrate class of this family. Typically, allenylzinc reagents exist in a solution as mixture of two rapidly interconverting metallotropic forms: the propargylic and the allenic one. When opposed to carbonyl derivatives (i.e., aldehydes, ketones, or imines), each form has the potential to undergo electrophilic substitution through an  $S_E2'$  mechanism providing either allenes (from

the propargylic form) or alkynes (from the allenic form). Lack of regioselectivity is thus a common drawback for such condensations [2].

A key feature of  $\alpha$ -silyl-substituted allenylzinc reagents is that the organosilyl group geminal to the carbon–zinc bond stabilizes the allenic form ( $\alpha$ -silicon effect) and thereby shifts the propargyl/allenyl metallotropic equilibrium toward the latter form (Scheme 1) [4]. Hence, condensation with carbonyl derivatives occurs with exquisite regioselectivity and affords exclusively the propargylic adducts [3,5]. Furthermore, in cases where two stereogenic centers are created during the condensation event, excellent levels of diastereocontrol are usually observed. In addition, their high functional-group tolerance and the fact that they lead to silylated alkynes that can be easily protodesilylated to unmask a terminal alkyne that then serves as handle for further synthetic elaboration are also important qualities of these propargylating reagents [6].

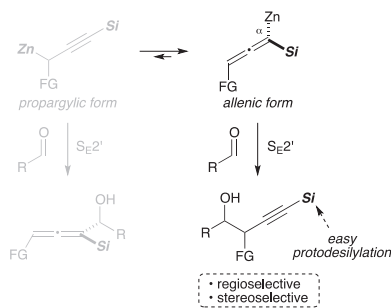
$\alpha$ -Substituted allenylmetals can be conveniently accessed by the 1,2-metalate rearrangement of alkynylous carbenoids. Commonly, migration of alkyl groups is

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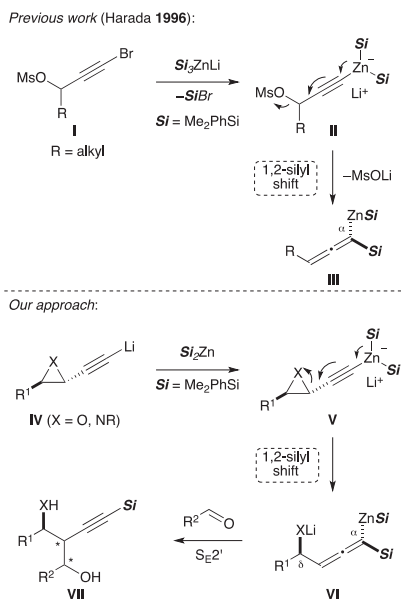
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**Scheme 1.** Condensation of aldehydes with  $\alpha$ -silyl-substituted propargyl/allenylic zinc reagents.

involved and  $\alpha$ -alkyl-substituted allenylmetals are obtained [7–10]. However, the approach is also suitable to access  $\alpha$ -silyl allenylmetals, but this prospect has remained so far virtually unexplored [10b,11]. In seminal studies, Harada et al. demonstrated that zincate complexes **II**, obtained from bromopropargyl mesylates **I** by halogen–metal exchange with  $(\text{Me}_2\text{PhSi})_3\text{ZnLi}$ , provided  $\alpha$ -silyl allenylzinc intermediates **III** after 1,2-migration of the organosilyl group with displacement of the propargylic leaving group through an  $\text{S}_{\text{N}}\text{i}$  mechanism (Scheme 2, top) [10b,12]. Inspired by these results and as part of our longstanding interest in ring-opening reactions of acetylenic epoxides [13] and aziridines [14], we reasoned that implementation of a similar approach with lithium alkynyl(disilyl)zincates **V** derived from those substrates and disilyl zinc reagents would lead to  $\delta$ -heteroatom substituted  $\alpha$ -silyl allenylzinc intermediates **VI** that could offer an expeditious stereoselective access to valuable 1,3-diols (**VII**,  $\text{X}=\text{O}$ ) or 1,3-aminoalcohols (**VII**,  $\text{X}=\text{NR}$ ) on condensation with aldehydes (Scheme 2, bottom). In this article, we describe our research endeavors in this area combining an overview of



**Scheme 2.** Formation of  $\alpha$ -silyl-substituted propargyl/allenylic zinc reagents by 1,2-metalate rearrangement of alkynylous carbenoids.

previous work on acetylenic epoxides [10e] and recent results on the ring-opening of *N*-*tert*-butanesulfonylaziridines and *N*-*tert*-butanesulfonylaziridines.

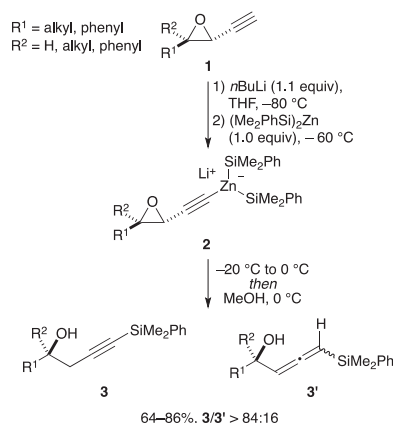
## 2. 1,2-Rearrangement of alkynyl(disilyl)zincates derived from acetylenic epoxides

Our first foray in this field was the result of our studies on the rearrangement of lithiated ethynylepoxides by reaction with dialkylzinc reagents [10e]. As part of this work, it was found that lithiated acetylenic epoxides also underwent transmetalation with  $(\text{Me}_2\text{PhSi})_2\text{Zn}$  at  $-60^\circ\text{C}$  to afford lithium alkynyl(disilyl)zincates **2** (Scheme 3). 1,2-Silyl migration inducing opening of the oxirane ring occurred on warming the reaction mixture to  $-20^\circ\text{C}$  and afforded the corresponding  $\alpha$ -silyl allenylzinc intermediates. After acidic aqueous workup, a mixture of homopropargylic (**3**) and allenic (**3'**) alcohols was obtained. The **3/3'** ratio was found to be highly dependent on the quench conditions and difficult to control. Ultimately, it was possible to find conditions to prepare regioselectively homopropargylic alcohols **3** using MeOH ( $0^\circ\text{C}$ ) to quench the reaction mixture after rearrangement. This optimized protocol was suitable for di- and tri-substituted acetylenic epoxides having either alkyl or aryl substituents and the corresponding alcohols **3** were obtained in 64–86% yield with good to excellent regioselectivity (**3/3'** > 84:16).

The possibility to use this chemistry to access 1,3-diols was also demonstrated. Condensation of propionaldehyde with the  $\alpha$ -silyl allenylzinc intermediate **2a'** (obtained from epoxide **1a**) was achieved at  $-40^\circ\text{C}$  and led to diol **4** [15] in a remarkable 78% yield with excellent regio- and stereoselectivity (Scheme 4). Trapping with acetone was less efficient and tertiary alcohol **5** was obtained in a lower 42% yield, still with excellent stereoselectivity. Interestingly, in the latter case, the presence of allenic regioisomers was also detected to some extent.

## 3. 1,2-Rearrangement of alkynyl(disilyl)zincates derived from acetylenic aziridines

Following on these results, we considered the rearrangement of acetylenic aziridines and focused on *N*-*tert*-



**Scheme 3.** Rearrangement of lithium alkynyl(disilyl)zincates.

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