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Intramolecular Carbolithiation of Silylated Enynes

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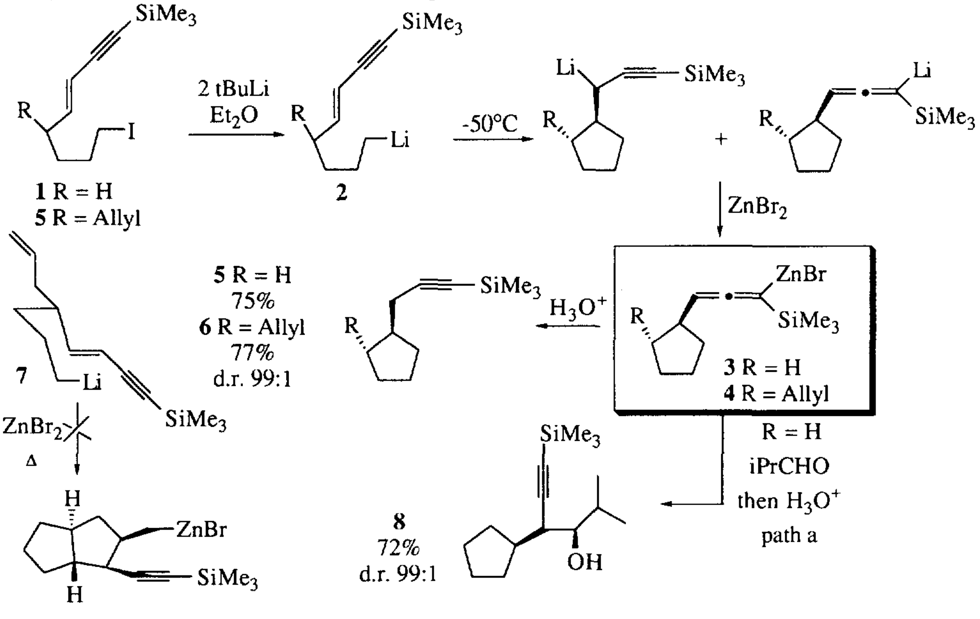
abstract: The intramolecular carbolithiation of silylated enynes was easily accomplished in a straightforward fashion, at low temperature and in modest to good yield for the synthesis of 4 and 5 membered rings. Copyright © 1996 Elsevier Science Ltd

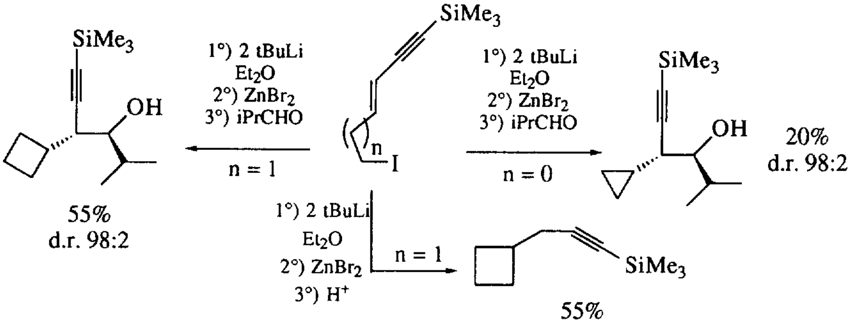
The highly stereoselective anionic cyclization of 5-hexenyllithiums to cyclopentylmethyl lithiums has attracted recent attention as a convenient route to polysubstituted cyclopentanes[1]. In the course of our research on the carbometalation reaction of silylated enynes, we have disclosed, in the preceding paper, a convenient intermolecular carbolithiation reaction[2]. In this note, we would like to report our preliminary results concerning the intramolecular carbolithiation reaction of silylated enynes. The requisite iodides **1** were treated with 2 equiv of t-BuLi in Et_2O at -78°C and the corresponding alkyllithiums **2** undergo a cyclization reaction at low temperature (< -50°C) to give the cyclic propargylic organolithiums which are in metallotropic equilibrium with the allenyl counterpart in a 60/40 ratio. However, addition of 1 equiv of zinc salt[3] to the mixture of allenyl/propargyl organolithium derivative and quenching with electrophiles only gives the propargylic isomers. The diastereoselectivity obtained from the reaction of **3** with isobutyraldehyde (path a) produces the *syn* homopropargylic alcohol **8** *via* a 6-membered ring transition state[3].



Scheme 1

The diastereoselectivity of this reaction was also studied by reaction of a substituted silylated enyne as described in scheme 1. The stereochemical outcome of this carbocyclization was interpreted by a chair-like transition state[1] in which the allyl substituent preferentially occupies a pseudo-equatorial position as in **7**. Considering this result and knowing that a propargylic zinc bromide undergoes a zinca-ene-allene cyclization[4] on a remote unsaturation, we tried to construct a *trans* fused bicyclooctane by adding a zinc salt solution. Unfortunately, even at 60°C in toluene, no *trans* bicyclo product was observed.

The intramolecular carbolithiations of alkenes for the synthesis of carbocycles of small size (cyclopropanes, cyclobutanes) are very rare due to the reversibility of this process[5]. Since, according to our strategy, a stabilized propargylic organolithium would result from the cyclization, we decided to test this possibility for cyclopropane and cyclobutane formation as described in scheme 2.



Scheme 2

Although the chemical yield is poor for the cyclopropane synthesis (during the iodine-lithium exchange, a metalation in allylic position compromises the clean generation of the corresponding organolithium derivative) and modest for the cyclobutane derivative, we are, however able to cyclize these sp^3 organolithiums (3-exo-Trig and 4-exo-Trig cyclization) to the thermodynamically favorable propargyl/allenyl organolithiums. By reaction with $ZnBr_2$ and isovaleraldehyde, the *syn* product was obtained in very good diastereomeric excess. In summary, the intramolecular carbolithiation of silylated enynes was easily accomplished in a straightforward fashion, at low temperature and in modest to good yield for the synthesis of 4 and 5 membered rings. The ease with which such cyclization is now possible is undoubtedly a consequence of the stabilization of the lithiated silyl propargyl system.

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