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Intermolecular Carbolithiation of Silylated Enynes

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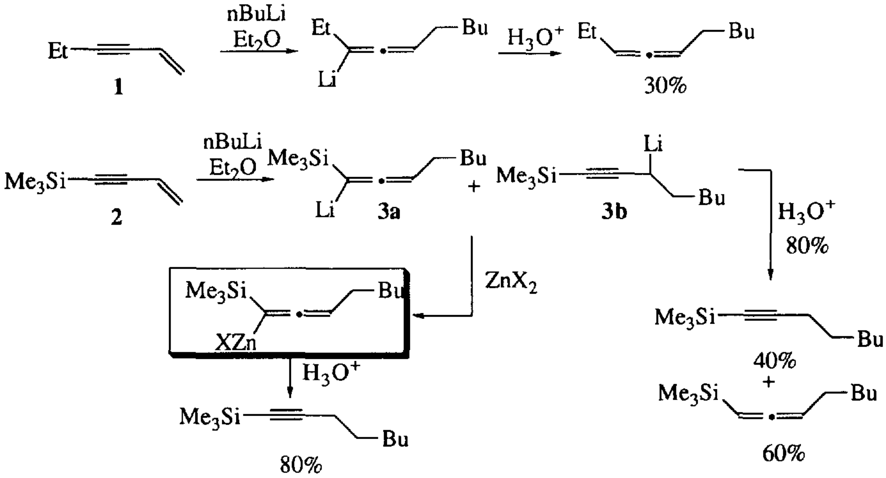
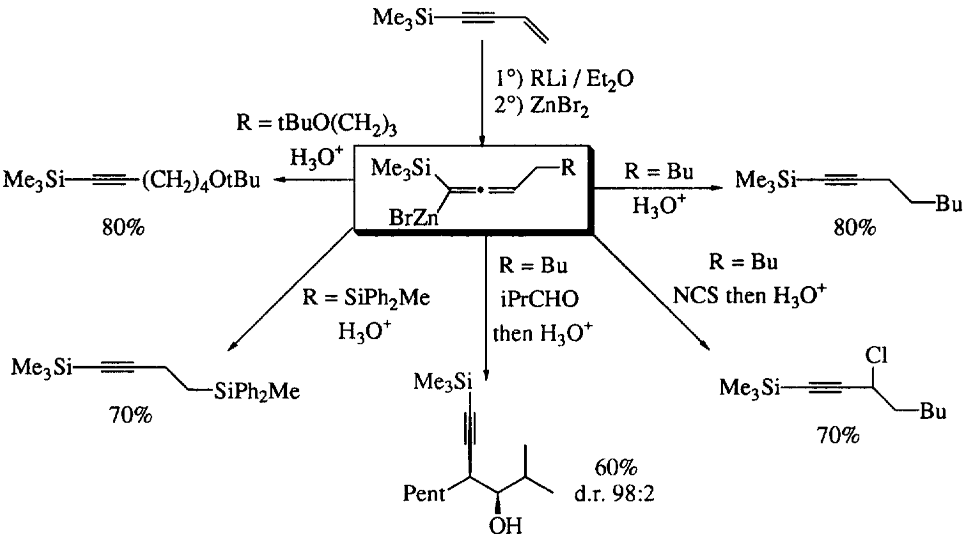
abstract: The presence of a trimethylsilyl group on the terminal sp carbon of an enyne promotes a very efficient carbolithiation of the C=C double bond leading to a propargylic-allenic lithium derivative, which in turn is converted to a single allenic zinc derivative.

Although some carbolithiation reactions of butadiene are known[1], the addition of lithium organometallics to unfonctionalized conjugated enynes provides a mixture of metalated propargylic and allenic isomers in low to moderate yields[2]. In the course of our research on the intramolecular carbometalation reaction of propargylic zinc derivatives, via the zinca-ene-allene reaction[3], we have been interested by the preparation of propargylic organometallic derivatives generated by the carbometalation reaction of enynes. To this end, we investigated the carbolithiation of silylated enynes, and we have found that the presence of silicon reinforces the substantial activation[4] already provided by the enyne system :



Scheme 1

The value of the silicon substituent in promoting the carbolithiation is pointed out by comparing the hex-1-en-3-yne **1** and the 1-(trimethylsilyl)-but-1-yn-3-ene **2** reactions with n-BuLi, as shown in scheme 1. However, to be synthetically usefull, the metallotropic equilibrium between the lithio allene **3a** and lithioalkyne **3b**[5] should be displaced by reaction with an electrophile in favor of only one derivative. Thus, as recently described[6], the addition of zinc salts to a mixture of **3a**/**3b** leads quantitatively to the allenyl zinc bromide intermediate and reaction of the latter with electrophiles, via a S_E2' process[7], only gives the propargylic derivative. This carbolithiation reaction of conjugated enynes allows the introduction of different alkyllithium derivatives, in the presence or absence of lithium salt and subsequently of different electrophiles[8]. Some typical examples are quoted in scheme 2.

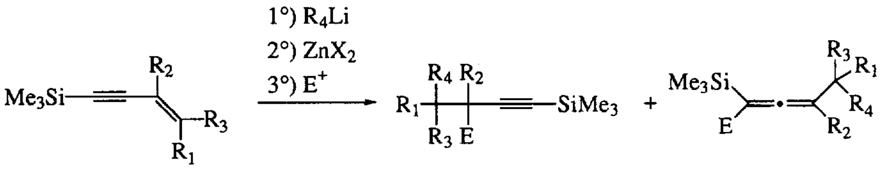


Scheme 2

The high diastereoselectivity, determined by ^1H and ^{13}C NMR on the crude mixture, obtained from the reaction of the allenyl zinc bromide with isobutyraldehyde to produce the *syn* homopropargylic alcohol is rationalized by the well known 6-membered ring transition state[6].

The scope of this reaction is quite broad : α-mono-, β-disubstituted silylated enynes as well as α-mono- and α,β-disubstituted silylated enynols are easily carbometalated as described in scheme 3, and the results are reported in Table 1.

The results reported here fulfill our expectations : the carbolithiation of polysubstituted silylated enynes gives, after the transmetalation step into the allenyl zinc bromide intermediate, the propargylic derivative. However, entry h and i point to another phenomenon that is the effect of the internal coordination of the resulting organometallic intermediate. In these cases, 25% of allenes are obtained as a mixture of two diastereoisomers in a 1:1 ratio. Moreover, by this methodology, the addition of MeLi (entry e) and the carbolithiation of a cyclic enyne (entry j) are impossible.



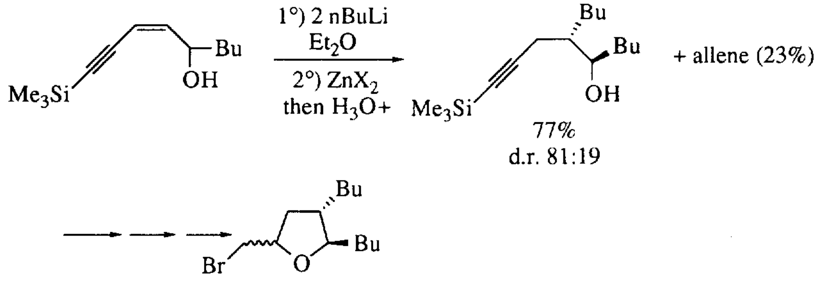
Scheme 3

Entry	R_1	R_3	R_2	R_4	E^+	% alcyne[b] (dr)	% allene[b] (dr)	yield[a]
a	H	H	Me	nBu	H^+	100	0	60%
b	H	H	Me	tBu	iPrCHO	100(82:18)	0	50%
c	H	H	pentenyl[d]	nBu	H^+	100	0	65%
d	H	H	pentenyl[d]	tBu	H^+	100	0	63%
e	H	H	pentenyl[d]	Me	H^+	-	-	-
f	H	butenyl[c]	H	nBu	H^+	100	0	69%
g	H	butenyl[c]	H	tBu	H^+	100	0	62%
h	CH_2OH	H	H	nBu	H^+	75	25(1:1)	70%
i	H	CH_2OH	Me	nBu	H^+	76	24(1:1)	50%
j	H	$(CH_2)_4$		nBu	H^+	-	-	-

a. Yield of isolated product. b. Diastereomeric ratio determined by NMR on the crude mixture. c. But-3-en-1-yl. d. Pent-4-en-1-yl.

Table 1

The diastereoselectivity of this reaction was also addressed by reaction of n-butyllithium with a secondary silylated *Z* enynol[9] as described in scheme 4.



Scheme 4

Here again, due to the presence of the alcoholate moiety, the propargylic isomer is obtained in 77% yield with 23% of the allenic isomer[10]. The diastereoselectivity of the propargylic derivative (81:19), determined after derivatization of the latter into a cyclic product, corresponds to an anti-Felkin approach[11].

The presence of a trimethylsilyl group on the terminal sp carbon of an enyne promotes a very efficient carbolithiation of the C=C double bond leading to a propargylic-allenic lithium derivative, which in turn is converted to a single allenic zinc derivative. This latter reacts, via a S_E2' process, to produce the fonctionalized propargylic isomer.

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8. The carbolithiation of the corresponding enynes in THF (instead of Et_2O as described in scheme 1) leads to only 16% of the carbometalated product. Moreover, no reaction was obtained by addition of an alkyl Grignard or alkyl zinc reagent, even at reflux of Et_2O
9. The same reaction on the E isomer does not lead to the carbometalated product.
10. The corresponding allenic system is obtained as a 1:1 mixture of diastereomer
11. Felkin, H. ; Swierczewski, G. ; Tambuté, A. *Tetrahedron Lett.* **1969**, 707-710. In fact this study concerns the n-BuLi, TMEDA addition to secondary allylic alcohols having a E double bond.

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