

GENERATION AND ALKYLATION REACTION OF 1-BROMOALKENYLZINCATE

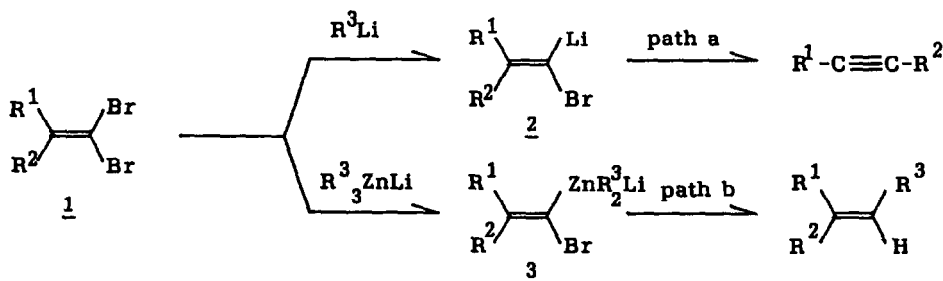
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Summary: 1-Bromoalkenylzincates ($R^1R^2C=CBzZnR^3_2Li$) which are generated by the reaction of 1,1-dibromoalkenes with a lithium triorganozincate (R^3_3ZnLi) at $-85\text{ }^\circ\text{C}$ undergo alkylation reaction at temperatures from $-85\text{ }^\circ\text{C}$ to $0\text{ }^\circ\text{C}$ to give alkenes $R^1R^2C=CHR^3$.

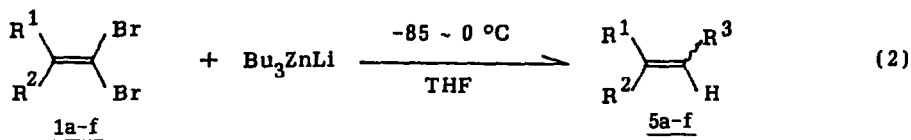
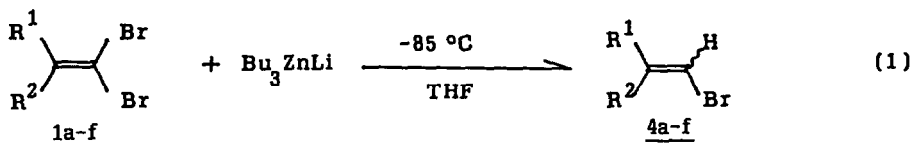
α -Haloalkyl- or α -haloalkenyllithium reagents (so-called lithium carbenoids) have ambiphilic nature: They not only react with various carbonyl compounds as the usual organolithium reagents but also act as α -lithiated electrophiles.^{1,2} In contrast to their nucleophilic nature hitherto widely applied for synthetic purposes,³ the electrophilic character of lithium carbenoids has not been fully utilized. Recently, Walborsky and co-workers have demonstrated that 1-bromoalkenyllithium undergoes nucleophilic substitution with *tert*-BuLi with a partial inversion of stereochemistry at the carbenoid carbon.¹ While their reaction may be utilized as a method of generating alkenyllithium in which an alkyl group is introduced at the α -position, its practical use is restricted unfortunately by the thermal instability of lithium carbenoid: 1-haloalkenyllithium **2** ($R^1, R^2 = \text{alkyl}$) readily dimerizes to give a butatriene and, moreover, when one of substituents R^1 and R^2 is H or phenyl, **2** undergoes Fritsch-Buttenberg-Wiechell rearrangement to give an alkyne (Scheme I, path a).⁴

Herein, we wish to report that 1-bromoalkenyl zincate **3** which is generated by the reaction of readily available 1,1-dibromoalkene **1**⁵ with triorganozincate is reasonably stable at $-85\text{ }^\circ\text{C}$ but undergoes a novel intramolecular alkylation reaction when the reaction mixture is warmed to $0\text{ }^\circ\text{C}$ (Scheme I, path b).

Scheme I

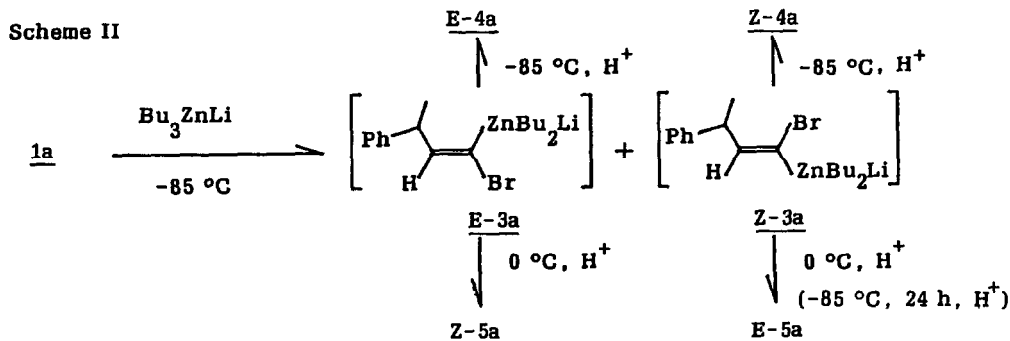


Treatment of 1,1-dibromo-3-phenyl-1-butene (1a) with $n\text{-Bu}_3\text{ZnLi}$ (1.2 equiv)⁶ in THF at $-85\text{ }^\circ\text{C}$ for 3 h followed by the addition of AcOH-THF gave 1-bromo-3-phenyl-1-butene (4a) ($\underline{E} : \underline{Z} = 2.6 : 1$) in 82% yield (eq 1, $\text{R}^1 = \text{Ph}(\text{CH}_2)_3\text{CH}-$, $\text{R}^2 = \text{H}$). When the above reaction mixture was gradually warmed to $0\text{ }^\circ\text{C}$ before the addition of AcOH-THF, 2-phenyl-3-octene (5a) ($\underline{E} : \underline{Z} = 1 : 1.8$) was obtained in 61% yield (eq 2, $\text{R}^1 = \text{Ph}(\text{CH}_2)_3\text{CH}-$, $\text{R}^2 = \text{H}$, $\text{R}^3 = n\text{-Bu}$).⁵ Intermediately formed 1-bromoalkenyl zincate 3a is considerably stable at $-85\text{ }^\circ\text{C}$; the treatment of 1a with Bu_3ZnLi at $-85\text{ }^\circ\text{C}$ for 24 h gave 4a (74% yield, $\underline{E} : \underline{Z} = 3.5 : 1$) with a small amount of butylated product 5a (10%, $\underline{E} : \underline{Z} = 33 : 1$).



The reversal of the $\underline{E} : \underline{Z}$ ratio in butylated product 5a (eq 2) from that in the bromoalkene 4a (eq 1) indicates that the alkylation proceeded with inversion of configuration at the carbenoid carbon, at least partly, through a Matteson-Pasto-type rearrangement (Scheme II).⁷ The increase in the $\underline{E} : \underline{Z}$ ratio of bromoalkene 4a in the reaction at $-85\text{ }^\circ\text{C}$ for 24 h, which was accompanied by the selective formation of by-product $\underline{E}\text{-5a}$, in comparison with the reaction for 3 h suggests that carbenoid $\underline{Z}\text{-3a}$ undergoes the rearrangement more readily than $\underline{E}\text{-3a}$.

Br/Zn exchange reactions proceeded not only with various 2-monosubstituted 1,1-dibromoalkene 1a-e but also with 2,2-disubstituted dibromoalkane 1f and the corresponding bromoalkene 4a-f was obtained after treatment with AcOH-THF at $-85\text{ }^\circ\text{C}$ (Table I). The reaction of 1a-c possessing such a relatively bulky substituent R^1 as secondary alkyl and phenyl group ($\text{R}^2 = \text{H}$) gave \underline{E} isomer of 4a-c selectively (entries 1, 6, and 8). Tributylzincate prepared by the reaction of $n\text{-BuMgCl}$ (3 equiv) with ZnCl_2 can also affect the Br/Zn exchange reaction (entry 2).

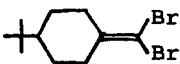


Reactions performed at temperatures from $-85\text{ }^{\circ}\text{C}$ to $0\text{ }^{\circ}\text{C}$ are also summarized in Table I. Under these conditions, not only *n*-butyl group but also other alkyl groups can be introduced by using the corresponding trialkylzincate. Even the introduction of *tert*-butyl group to 2,2-disubstituted 1f proceeded effectively to give 5f ($\text{R}^3 = \textit{tert}$ -butyl) in 60% yield (entry 16).

The reactivity of triorganozincate toward 1,1-dibromoalkenes deserves comparison with that of organocuprate. In this regard, Posner et al. reported the dimethylation reaction of 2,2-disubstituted dibromoalkene with Me_2CuLi .^{5b} For comparison, we carried out the reaction of 2-monosubstituted dibromoalkene 1a with dibutylcopperlithium in THF at $-85\text{ }^{\circ}\text{C}$ for 2 h. The reaction gave 3-phenylbutyne (76%) but neither bromoalkene 4a nor the dibutylated product was formed.

In summary, we described a novel method for the generation of 1-bromoalkenylzincate 3 and its alkylation reaction. Organozinc reagents generated after the alkylation reaction can be utilized as versatile alkenylating reagents and works are in progress under these lines.

Table I Reaction of Dibromoalkene with Lithium Trialkylzincate

Entry	Dibromoalkene (R^1, R^2)	R^3_3ZnLi (R^3)	Reaction Temp. ($^{\circ}\text{C}$)	Product	Yield ^a (%)	[<u>E</u> : <u>Z</u>] ^a
1	<u>1a</u> (Ph(CH ₃)CH-, H)	<i>n</i> -Bu	-85	<u>4a</u>	82	[2.6 : 1]
2 ^b	<u>1a</u>	<i>n</i> -Bu	-85	<u>4a</u>	60	[7.8 : 1]
3	<u>1a</u>	<i>n</i> -Bu	-85 - 0	<u>5a</u> ($\text{R}^3 = \textit{n}$ -Bu)	61	[1 : 1.8]
4	<u>1a</u>	<i>s</i> -Bu	-85 - 0	<u>5a</u> ($\text{R}^3 = \textit{s}$ -Bu)	83	[1.2 : 1]
5	<u>1a</u>	<i>t</i> -Bu	-85 - 0	<u>5a</u> ($\text{R}^3 = \textit{t}$ -Bu)	18	[8.4 : 1]
6	<u>1b</u> (c-C ₆ H ₁₁ , H)	<i>n</i> -Bu	-85	<u>4b</u>	33	[2.4 : 1]
7	<u>1b</u>	<i>n</i> -Bu	-85 - 0	<u>5b</u> ($\text{R}^3 = \textit{n}$ -Bu)	58	[1 : 1.2]
8	<u>1c</u> (Ph, H)	<i>n</i> -Bu	-85	<u>4c</u>	97	[3.6 : 1]
9	<u>1c</u>	<i>n</i> -Bu	-85 - 0	<u>5c</u> ($\text{R}^3 = \textit{n}$ -Bu)	24	[1 : 4.1]
10	<u>1d</u> (Ph(CH ₂) ₂ -, H)	<i>n</i> -Bu	-85	<u>4d</u>	66	[1.1 : 1]
11	<u>1d</u>	<i>n</i> -Bu	-85 - 0	<u>5d</u> ($\text{R}^3 = \textit{n}$ -Bu)	72	[ca. 1 : 1]
12	<u>1e</u> (BnO(CH ₂) ₂ -, H)	<i>n</i> -Bu	-85	<u>4e</u>	83 ^c	[1.0 : 1]
13	<u>1e</u>	<i>n</i> -Bu	-85 - 0	<u>5e</u> ($\text{R}^3 = \textit{n}$ -Bu)	82 ^c	[1.0 : 1]
14	<u>1f</u> 	<i>n</i> -Bu	-85	<u>4a</u>	46	
15	<u>1f</u>	<i>n</i> -Bu	-85 - 0	<u>5f</u> ($\text{R}^3 = \textit{n}$ -Bu)	64	
16	<u>1f</u>	<i>t</i> -Bu	-85 - 0	<u>5f</u> ($\text{R}^3 = \textit{t}$ -Bu)	60	

^aUnless otherwise noted, yields and E : Z ratios were determined by GLC.

^bTributylzincate prepared by the reaction of *n*-BuMgCl with ZnCl_2 was employed.

^cIsolated yield.

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References and Notes

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