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ZIRCONIUM-CATALYZED ALLYLALUMINATION AND BENZYLALUMINATION OF ALKYNES[1]

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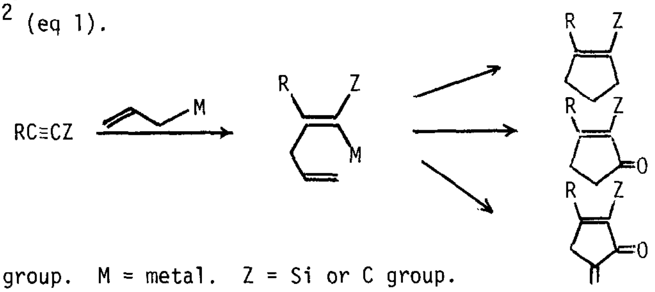
SUMMARY: Allylalanes or benzylalanes react with either terminal or internal alkynes in the presence of a catalytic amount of Cl_2ZrCp_2 to produce in high yields cis-carboalumination products.

We have recently demonstrated that allylmetallation of alkynes is useful for preparing various cycloalkenes[2] (eq 1).

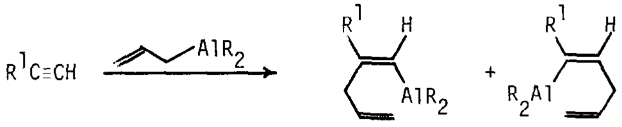


(1)

R = C group. M = metal. Z = Si or C group.

Unfortunately, however, the synthetic utility of this methodology has been limited by the fact that clean and selective allylmetallation of alkynes has been difficult in many cases.[3] Although we recently developed satisfactory procedures for allylzincation of silylated 1-alkynes[2,4] and Zr-promoted allylzincation of internal alkynes,[2] conversion of terminal alkynes into allylmetallated species uncomplicated by other side reactions has not been achieved except in some special cases. Thus, the reaction of terminal alkynes with allylzinc halides developed by Gaudemar and Miginiac[5] is complicated by alkyne proton abstraction as well as by double allylmetallation which often is the major course of reaction. Mikhailov's allylboration[6] appears to proceed well only with highly reactive terminal alkynes, such as alkynyl ethers. With "ordinary" terminal alkynes, such as 1-octyne, allylboration is evidently complicated by competitive cyclization.[7]

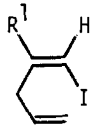
We now report that allylalanes, e.g., allyldiisobutylalane, undergo allylalumination with terminal alkynes in the presence of Cl_2ZrCp_2[8] to produce exclusively cis-monoallylation products (>98% Z) as ca. 75:25 mixtures of two regioisomers **1** and **2** (eq 2).



1 2

(2)

Internal alkynes react in a similar manner, although 1-silyl-1-alkynes do not. We further report that treatment of a mixture of **1** and **2** with a deficient quantity, e.g., 0.6-0.7 equiv, of iodine can provide isomerically ≥98% pure 1-iodo-1,4-pentadiene derivative 3 typically in 50-70% yields based on the starting 1-alkyne. This procedure thus provides, for the first time, a highly selective method for converting terminal alkynes into various types of 1,4-pentadiene derivatives 4, that appears to be general with respect to the alkyne structure and uncomplicated by side reactions.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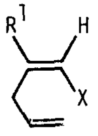
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(X = C or hetero atom group)

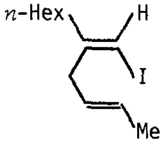
Our earlier attempts to achieve allylalumination with allylaluminum sesquibromide were largely unsuccessful.[2a] Crucial to the development of a reproducible and satisfactory procedure is controlling the amount of ether present in the carbometallation mixture. Typically, the reaction of allylmagnesium bromide with i-Bu_2AlCl in ether followed by evaporation of ether at 50°C and 0.1 mm for 1-2 h provides a mixture containing allyldiisobutylalane and ether in an essentially 1:1 ratio, as judged by its ^1H NMR spectrum, although it is not clear whether the ether showing the methylene quartet at 3.79 ppm is complexed with Al or Mg. The reaction of this mixture with 1-octyne (allylmagnesium bromide/1-octyne = 1.1) in 1,2-dichloroethane in the presence of Cl_2ZrCp_2 (1 equiv) gives a ca. 75:25 mixture of 1a and 2a ($R = i$-Bu, $R^1 = n$-Hex) in nearly quantitative yield in 1-2 h at room temperature. When the removal of ether (ca. 20 equiv) is omitted, however, no reaction occurs even after 24 h. Addition of even one equiv of ether to the evaporated mixture significantly slows down the desired reaction and limits the carbometallation yield to ca. 50% (after 24 h). Strikingly, there is no indication of either addition of the i-Bu-Al bond or Zr-catalyzed hydroalumination,[9] indicating that the allyl group is far more reactive than i-Bu. Although the use of one equiv of Cl_2ZrCp_2 is advantageous in promoting allylalumination, the use of 5-10 mol % of Cl_2ZrCp_2 will lead to a high-yield conversion that usually requires 1-2 days at room temperature, clearly indicating that the reaction is catalytic in Cl_2ZrCp_2.

In contrast with the allylzincation reaction of 1-silyl-1-alkynes,[2a,4] which is essentially 100% regioselective but only ca. 85% stereoselective, the Zr-catalyzed allylalumination reaction of terminal alkynes is >98% stereoselective, as judged by ^{13}C and ^1H NMR. The cis addition reaction was expected on the basis of related results obtained earlier.[8] The Z geometry of 3a ($R^1 = n$-Hex) was established by converting 1-iodo-1-trimethylsilyl-2-(n-hexyl)-1,4-pentadiene,[2a] which was ca. 85% Z, to 3a (ca. 90% Z) by treatment with NaOMe-MeOH, which was known to proceed with retention.[10]

The scope and synthetic utility of the Zr-catalyzed allylalumination are indicated by the results summarized in Table I. The presence of an alkenyl or silylated alkynyl group does not interfere with the desired allylalumination. In view of the highly satisfactory results in obtaining isomerically pure alkenyl iodides by controlling the amount of iodine, we applied this procedure to the case of alkylalumination, which also gives ca. 75:25 mixtures of terminally and internally metallated alkenylalanes.[11] The reaction of 1-octyne with n-Pr_2AlCl-Cl_2ZrCp_2, followed by quenching with 0.7 equiv of iodine, produced an 88:12 mixture of (E)-1-iodo-2-(n-propyl)-1-

octene and (*E*)-5-iodo-4-undecene in 61% combined yield. Although enrichment of the terminally functionalized isomer does occur, it is not as effective as in the cases of allylalumination.

We earlier suggested that allylzincation of terminally silylated alkynes, which proceeds with clean allylic rearrangement, might proceed via a six-centered transition state, whereas Zr-promoted allylzincation of internal alkynes without allylic rearrangement might be a four-centered process.[2a] To probe the regiochemistry of the Zr-catalyzed allylalumination reaction, we reacted 1-octyne with (*E*)-crotyldiisobutylalane and Cl_2ZrCp_2. After protonolysis with dil HCl, a ca. 75:25 mixture of (*E*)-2-(*n*-hexyl)-1,4-hexadiene and (2*E*, 5*E*)-2,5-dodecadiene was obtained in 60% yield along with 1-octene (16% yield) indicating that, in this case, the *i*-Bu group competed with the allyl group and participated in hydrometallation.[9] Iodinolysis of the mixture with 0.5 equiv of iodine yielded isomerically pure (>98%) **5** in 45% yield. This difficulty was, however, readily circumvented by using (*E*)-crotyldimethylalane. In this case, the combined yield of carboalumination was 95%, and iodinolysis with 0.65 equiv of iodine gave **5** in 61% yield, even though a minor amount (ca. 5%) of unidentified byproduct, which does not appear to be isomeric with **5**, was present. None of the allylic rearrangement product, i.e., **6**, was obtained. The observed regiochemistry suggests that the reaction may proceed via a four-centered transition state.



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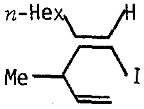

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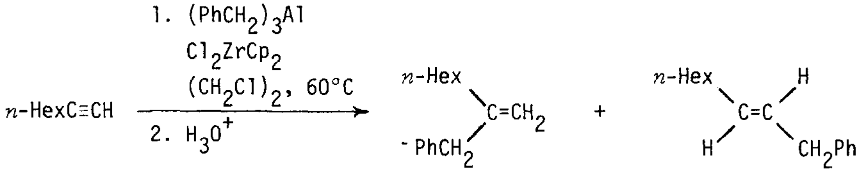
The favorable results obtained in allylalumination prompted us to investigate the Zr-catalyzed reaction of alkynes with other types of organoalanes. The reaction of 1-octyne with tribenzylalane and Cl_2ZrCp_2 was sluggish at room temperature. At 60°C, however, a 70:30 mixture of 2-benzyl-1-octene and (*E*)-1-phenyl-2-nonene was obtained in 94% combined yield in 48 h.



$$n\text{-HexC}\equiv\text{CH} \xrightarrow[\text{2. } H_3O^+]{\text{1. } (PhCH_2)_3Al,\ Cl_2ZrCp_2,\ (CH_2Cl)_2,\ 60°C} \underset{PhCH_2}{\overset{n\text{-Hex}}{>}}C{=}CH_2 + \underset{H}{\overset{n\text{-Hex}}{>}}C{=}C\underset{CH_2Ph}{\overset{H}{<}} \qquad (3)$$

94% (70:30)

The use of benzyldimethylalane in place of tribenzylalane in this reaction led to the formation of benzylmetallated products (a 70:30 regioisomeric mixture) and a methylmetallated product in 40 and 47% yields, respectively. On the other hand, the use of benzyldiisobutylalane induced only hydrometallation producing 1-octene after protonolysis. Triphenylalane-Cl_2ZrCp_2 did not react with 1-octyne even at 60°C. We are currently investigating in detail these and related carbometallation reactions.

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Table I. Allylalumination of Alkynes[a]

Alkyne	Allylating agent	Time(h)	Allylmetalation product		Iodinolysis product		
			Yield[b](%)	Regioisomeric purity (%)	Iodine(equiv)	Yield[c](%)	Isomeric purity(%)
n-HexC$\equiv$CH	I[d]	1	99	72	0.7	64	98
n-HexC$\equiv$CH	II[e]	1	98	75	-	-	-
$CH_2{=}CH(CH_2)_4C\equiv CH$	I	1	95	75	0.7	65	98
$Me_3SiC\equiv CCH_2C\equiv CH$	I	2	99	65	0.6	53	>98
PhC$\equiv$CH	I	1	90	>98	1.2	86	>98
n-BuC$\equiv$CBu-n	I	18	73	-	1.2	69	>99
n-HexC$\equiv$CSiMe$_3$	I	18[f]	<1	-	-	-	-

[a] Unless otherwise mentioned, the reaction was carried out at room temperature in $(CH_2Cl)_2$ in the presence of one equiv of Cl_2ZrCp_2 using 1.1 equiv of an allylalane. All isolated products yielded satisfactory spectral data. [b] Based on GLC analysis of protonolysis products. [c] Isolated yield. [d] Allyldiisobutylalane. [e] Allyldimethylalane. [f] No reaction was observed even after 18 h at 60°C.

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7. This summary statement does not exclude special cases of monoallylmetallation of terminal alkynes. For example, *E*-cinnamylzinc bromide reacts with acetylene itself to give a monocarbometallation product in 66% yield [Frangin, Y.; Gaudemar, M. *Bull. Soc. Chim. Fr.* 1976, 1137].
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