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# MAO-Catalyzed Allylzirconation of 1-Alkynes

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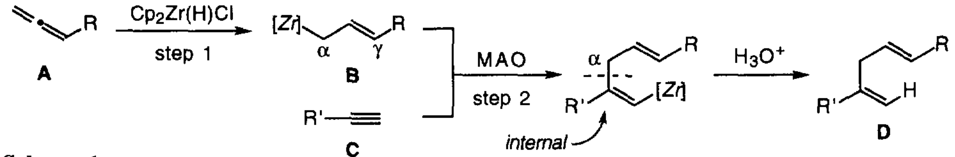
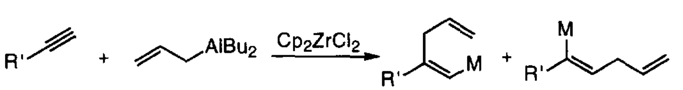
**Abstract:** A regio- and stereocontrolled method for the allylmetallation of 1-alkynes is described. The allylzirconium species, generated by hydrozirconation of allenes, undergo regioselective addition to 1-alkynes in the presence of organoaluminum reagents among which methylaluminoxane (MAO) is particularly effective. © 1997 Elsevier Science Ltd.

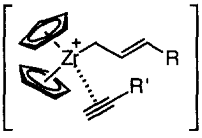
The present communication describes a regio- and stereocontrolled reductive coupling of allenes and alkynes via two steps: (1) hydrozirconation of allene **A** to generate allylzirconium species **B** (step 1),[1,2] and (2) the carbometallation[3] of alkyne **C** with **B** (step 2) promoted by methylaluminoxane (MAO) (Scheme 1). The overall reaction gives, among many possible isomers, the "α–internal" coupling product **D** in high selectivity. Discussed herein is how this two-step process was established, inspired by the implication from Ziegler–Natta or Kaminsky polymerization that could be viewed as the repeated carbometallation.[4]



**Scheme 1** [Zr] = $Cp_2(Cl)Zr$



(1)

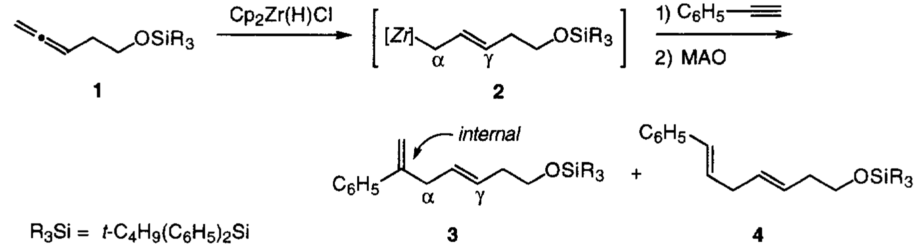


**E**

To begin with, we considered the viability of two elementary reactions. While step 1 is based on our recent finding,[1] step 2 is a carbometallation reaction, which is a subject of current interest in organic synthesis.[3,5] An important precedent related to the latter step is the pioneering work of Negishi (eq. 1):[6] an allylaluminum adds to alkyne aided by catalytic or preferably stoichiometric $Cp_2ZrCl_2$. We attempted the reaction of allylzirconium **B** and alkyne **C**, which, however, did not proceed at all (see Table 1, next page). At this stage, we focused our attention on the cationic zirconocene or hafnocene species that could activate various Lewis basic functionalities.[1b,4b,7,8] Our hope was centered on their ability to activate alkenes and alkynes, which is well-recognized in the polymer field.[4] More precisely, we hoped that such cationic species would facilitate the assembly and the activation of the allylzirconium moiety and alkyne as shown in **E**. Along these lines, we examined additives that would generate a cationic zirconocene species from **B**.

Allene **1**[9] was subjected to hydrozirconation ($Cp_2Zr(H)Cl$[10] / $CH_2Cl_2$, –78 °C → 25 °C),[1c] and the resulting red solution of allylzirconium **2** was chilled to –78 °C, to which was added ethynylbenzene. No reaction occurred at this stage or even after the temperature was raised (run 1). As discussed before, we screened additives that could serve to generate a cationic zirconocene species. While silver salts, such as $AgClO_4$, were incapable of promoting the allylmetallation even at 25 °C, we were pleased to find that organoaluminums are the reagents of choice: a mixture of **2** and ethynylbenzene was treated with $Et_3Al$ at –78 °C, and the temperature was allowed to rise rather quickly (–78 → 25 °C during 20 min).[11] TLC-Monitoring showed that the reaction starts to proceed around 0 °C, and further stirring at 25 °C gave a regioisomeric mixture of heptadienes, **3** and **4**, in 90% combined yield (run 2).[12] Furthermore, an analogy to the Kaminsky system led us to examine the use of methylaluminoxane (MAO)[4,13] which turned out to be extremely effective. The carbometallation proceeded in the temperature range of –25 to –20 °C, substantially lower than the case of $Et_3Al$, and the yield as well as the regioselectivity were further improved to give **3** almost exclusively (run 3).[14]

**Table 1**



| Run | Catalyst | Reaction Temp./ °C | Yield/% | Regioselectivity **3/4** |
|---|---|---|---|---|
| 1 | — | –78 → +25 | — | — |
| 2 | $Et_3Al$[a] | –78 → +25 | 90 | 9/1 |
| 3 | MAO[b] | –78 → –20 | 93 | 13/1 |

[a] 0.3 equiv. [b] 0.3 equiv. in Al-unit (see refs. 12,13)

The product **3** is the one arising from the C–C bond formation between *the internal carbon of the alkyne* and *the α position of the allylzirconium*. Also notable is that this "α–internal product" is exclusively *trans* with respect to the geometry of the double bond derived from the allylzirconium.

The mode of the allylzirconium addition to the C≡C bond is *cis* as evidenced by NOE study (Fig. 1). Upon quenching the reaction with $CH_3OD$, $H_a$ was replaced by a deuterium (90% incorporation).

The regioselectivity of the allyl moiety (α) is in line with the Negishi reaction (eq. 1),[6] and stands in contrast to the γ-selectivity of various other methods recently reported.[5]

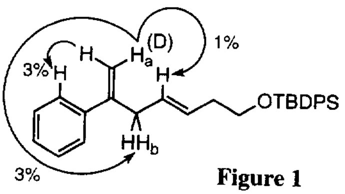
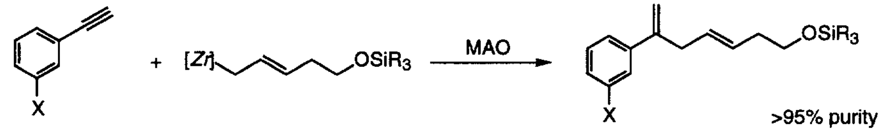


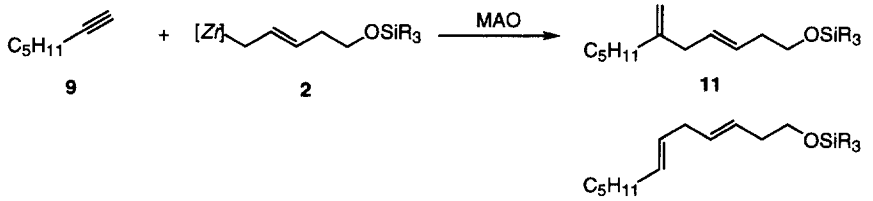
**Figure 1**

The MAO-catalyzed reactions were further applied to various substrate combinations, where the regio- and stereochemical features described above, *i.e.*, α–internal–*trans*, proved valid for most of the cases examined. For example, the reactions of allylzirconium **2** (vide supra) with aryl-acetylenes, **5** and **6**, were smooth and even more selective to give the 1,4-diene products **7**, **8** in >95% isomeric purity, respectively (eq. 2).[15]

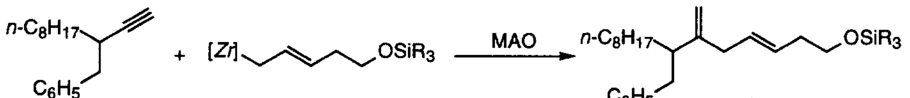


**5** X = Cl
**6** X = OMe
**2**
**7** X = Cl 95%
**8** X = OMe 94%
>95% purity
(2)

As for the acetylenes armed with an alkyl group, the regioselectivity depends on the alkyl substituent. Acetylene **9** with a *primary* alkyl substituent gave a mixture of **11** (*internal*) and **12** (*terminal*) in a ratio of 4/1 ($^1$H NMR) (eq. 3),[15] while excellent regioselectivity was observed for acetylene **13** bearing a *branched* alkyl group to give product **14** in high yield (eq. 4).[16] Thus, the steric bulk of the alkyne substituent affects the regioselectivity, although the effect from the electronic origin remains to be clarified (*cf.* eqs. 2, 5).

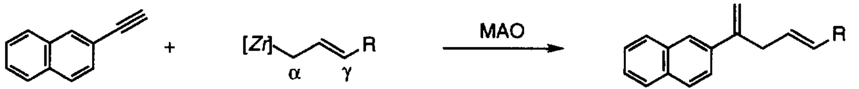


**9** **2** **11** **12**
(82% combined yield, **11**/**12** = 4/1)
(3)



**13** **2** **14** 94%
>95% purity
(4)

It was also found that various allenes smoothly take part in the present reaction. Aryl- or alkyl-substituted allylzirconiums, generated from allenes **15–17**, underwent selective coupling at the α-end, and the adducts **18–20** were obtained in high yields and uniformly with high isomeric purity (eq. 5).



**15**
>95% purity
(5)

**16** R = $C_6H_5$ 69%
**17** R = *cyclo*-$C_6H_{11}$ 94%
**18** R = *n*-$C_7H_{15}$ 99%

In comparison with the previous methods for the allylmetallation of alkynes,[5,6] the present method has an obvious advantage in terms of the broad applicability to various allene–alkyne combinations to allow the synthesis of various 1,4-dienes in high yields. Methylaluminoxane (MAO), which has been utilized only in polymerization chemistry,[4] was found to serve as an efficient promoter for the present reaction.[17]

In conclusion, the regio- and stereocontrolled carbometallation of alkynes with allylzirconiums is described. Further studies on the mechanistic as well as the synthetic aspects of the present reaction are now in progress in our laboratory.

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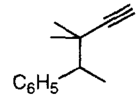
11. When the temperature was raised more slowly (–78 to 25 °C during 1 h), the yield was lower (66%).
12. Ethylation product was not observed.
13. Modified MAO [the hydrolysate of Me$_3$Al and*i*-Bu$_3$Al (2:1), Al = 6 wt% in toluene, mw ≈ 1200] was used throughout this study, which was kindly donated from Tosoh Akzo Co.
14. Typical procedure is described for the reaction of ethynylbenzene and allene **1**: To a suspension of Schwartz' reagent,[10] prepared by adding CH$_2$Cl$_2$ (0.7 mL) to Cp$_2$Zr(H)Cl (198 mg, 0.767 mmol) at –78 °C,[1c] was added allene **1** (209 mg, 0.647 mmol) in CH$_2$Cl$_2$ (2.5 mL), and the mixture was warmed to 25 °C over 20 min and further stirred for 30 min. The resulting red solution was chilled to –78 °C, to which was added ethynylbenzene (39.2 mg, 0.384 mmol) in CH$_2$Cl$_2$ (2.5 mL) followed by modified MAO (0.93 M, 0.12 mL, see ref. 13). After the mixture was warmed to –20 °C over 15 min, and stirred for 20 min at this temperature, the reaction was stopped by careful addition of sat. K$_2$CO$_3$ solution. The mixture was stirred for 5 min at room temperature, to which was added anhydrous Na$_2$SO$_4$. After filtration through a Celite pad and evaporation, the crude products were purified by silica-gel column chromatography (hexane/CHCl$_3$= 9/1) to give the isomeric mixture of heptadienes **3**,**4** (152 mg, 93%, **3**/**4** = 13/1).[15]
15. For **18**, **19** and **20**, the regio- and stereoselectivity was determined by $^1$H NMR and capillary GC analysis. The *E*/*Z* assignment was based on the extensive decoupling study. For silyloxydienes **3**, **7**, **8**, **11**, **12** and **14**, the structures were determined for the alcohols obtained by removal of the silyl group (TBAF).
16. The reaction with a *tert*-alkyl-substituted alkyne (e.g., **21**) was sluggish.
17. We thank one of the referees who suggested a possible mechanism that includes an allylaluminum species generated by the Zr$\rightarrow$Al transmetallation. However, we have obtained a good deal of evidence to rule out this possibility, since similar reactivity was observed even when an aluminum-free promoter, instead of MAO, was employed, such as (C$_6$H$_5$)$_3$CB(C$_6$F$_5$)$_4$ (unpublished result of S. Yamanoi).



**21**

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