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Regioselectivity of MAO-Catalyzed Allylmetallation of Conjugated Enynes with Allylzirconiums

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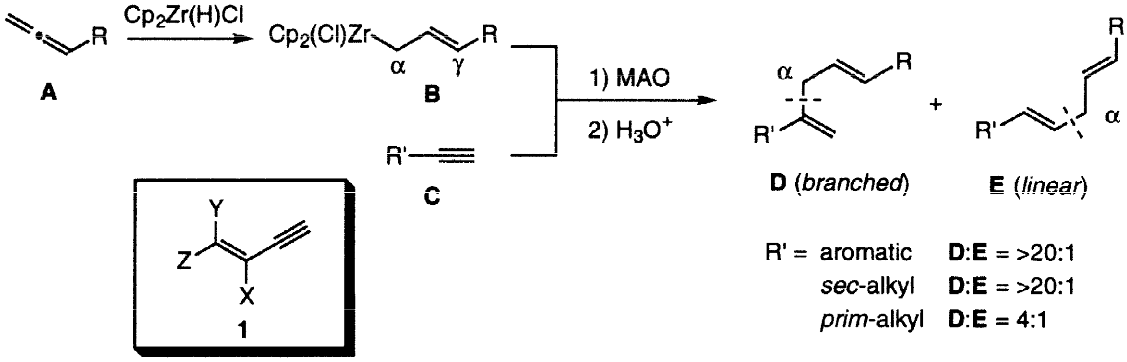
Abstract: Various conjugated enynes **1** were subjected to the MAO-catalyzed reaction with the allylzirconium, generated by hydrozirconation of allenes. In light of the regiochemisty, the C–C bond formation occurs exclusively between the α carbon of the allylzirconium and the "yne" part of the conjugated enyne **1**. Steric demand of the α-substituent X in **1** is the decisive factor for determing the the reactive site for **1**. © 1998 Elsevier Science Ltd. All rights reserved.

We recently reported a method for allylation of 1-alkynes (Scheme 1):[1] Allylzirconium **B**, generated by the hydrozirconation of allene **A**,[2] adds to alkyne **C** in the presence of an organoaluminum promoter, e.g. methylaluminoxane (MAO).[3] As for the regiochemistry, allylzirconium **B** undergoes the C–C bond formation exclusively at the α carbon. On the other hand, the reactive site for the alkyne partner **C** depends on the steric demand of the substituent R': When R' is an aromatic or a *sec*-alkyl group, the internal carbon of alkyne **C** is the exclusive allylation site to give the "branched" 1,4-diene **D**, whereas a minor amount of the "linear" product **E** is also produced when R' is a sterically less demanding group, i.e. a *prim*-alkyl (see below).



Scheme 1

With this tendency in mind, we became interested in the reaction of conjugated enynes of the general formula **1** with varying substituents (X, Y, Z) to examine the regiochemical outcome. An additional interest in such enyne substrates was the possible participation of the "ene" part as a reactive site for the allylmetallation.[4,5] In this communication, we describe the results of this study that can be summarized as

(1) the C–C bond formation occurs exclusively at the "yne" part in **1**,

(2) the regioselectivity within the "yne" part depends critically on the presence/absence of the substituent X.

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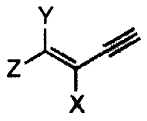
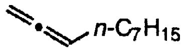
The allyzirconium species used for the present study was generated, as reported previously,[2] from allene **2** (TBDPS = t-$C_4H_9(C_6H_5)_2Si$) or **3** by hydrozirconation[6] ($Cp_2Zr(H)Cl$/ CH_2Cl_2, −78 °C → 25 °C), which was allowed to react with various enynes **1a–1f** as described below.



1

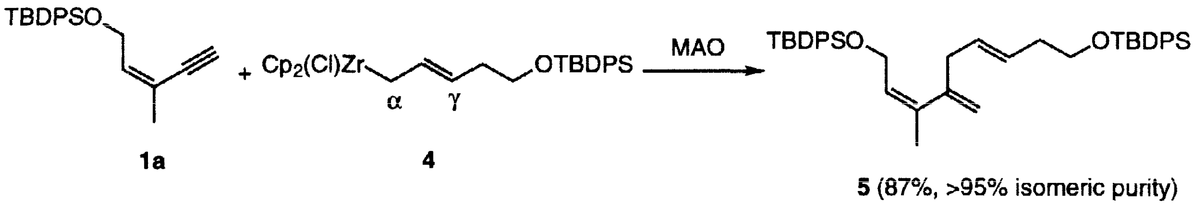
2



3

Enynes with the "α-substituent" (X ≠ H in 1)

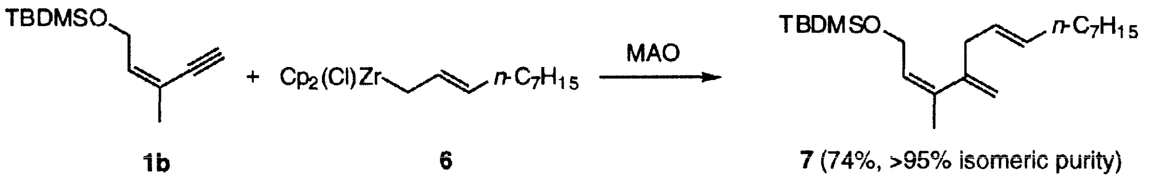
Eq. 1 represents the reaction of the enyne with an "α-substitutent", which was fully regioselective. The allylzirconium species **4**, generated from allene **2**, was chilled to −78 °C, to which was added enyne **1a**. After the addition of MAO (0.3 equiv., toluene solution),[3,7] the temperature was raised to −25 °C during 15 min,[8] and the mixture was further stirred for 15 min. Aqueous workup[1] afforded triene **5** as a sole product (^{1}H NMR and HPLC).[9,10]



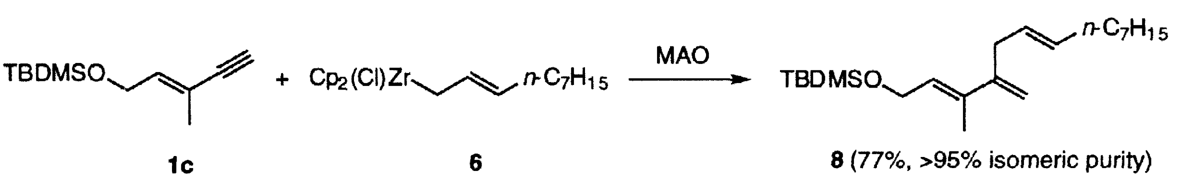
(1)

Two points are noteworthy: (1) The allylzirconium species **4** reacted exclusively at its α position, and the geometry of the double bond derived from this partner proved *trans* (J = 15.2 Hz). (2) The enyne substrate **1a** underwent the reaction, not at the C=C bond, but at the C≡C bond with the C–C bond formation at its internal carbon, giving the branched isomer (corresponding to **D** in Scheme 1).

It was noted that, in such branched products, the original geometry of the enyne double bond was retained as illustrated by eqs. 2 and 3. Upon reaction with allylzirconium **6**, generated from allene **3**, the (*Z*)-enyne **1b** [N.B. the silyl group is a TBDMS (= t-$C_4H_9(CH_3)_2Si$)] gave triene **7** (eq. 2),[10] whereas the (*E*)-enyne **1c** was cleanly converted to isomeric product **8** as a single isomer (eq. 3).[10] Thus, the enyne substrates with the α-substituent undergo the allylmetallation in a fully regio- and stereocontrolled manner (cf. the cases for enynes without the "α-substituent", eqs. 5 and 6).

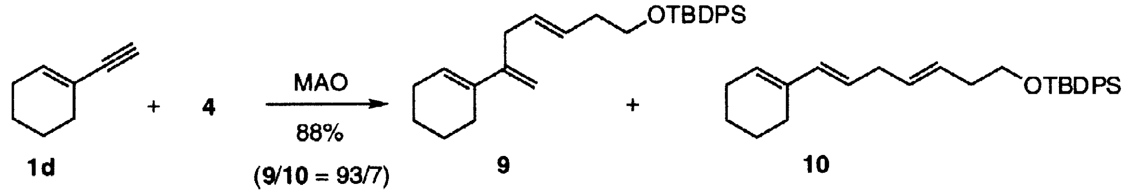


(2)



(3)

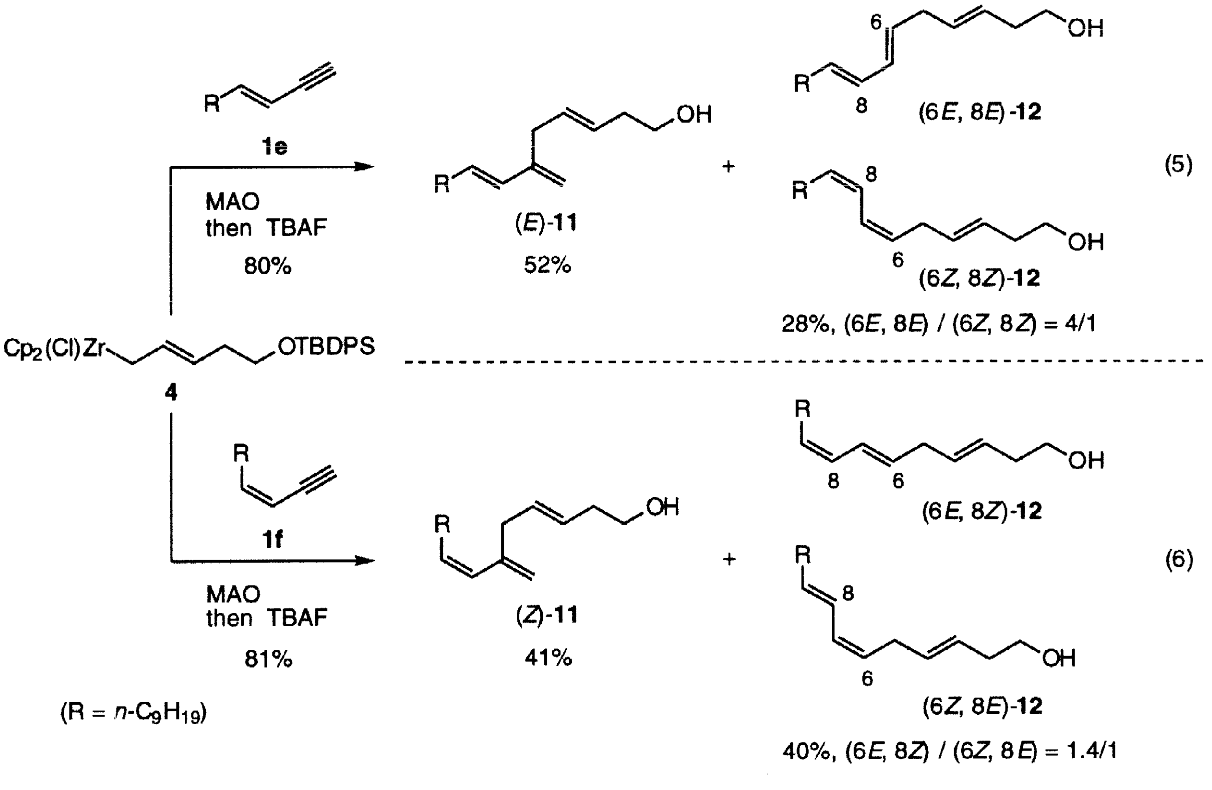
Even though having the "α-substituent", cyclic enyne **1d** showed a slightly decreased regioselectivity upon subjected to the reaction with **4** (eq. 4). In addition to the branched product **9**, a small amount of the linear product **10** was also produced, due presumably to the reduced steric demand by a cyclic structure.



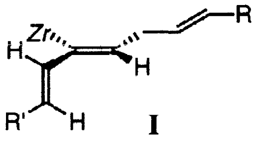
(4)

Enynes without the "α-substituent" (X = H in 1)

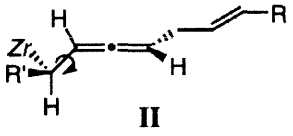
The enyne substrates lacking the α-substituent showed, not unexpectedly, poor regioselectivities. However, an interesting observation was made with respect to the olefinic geometry of the products. Upon reaction of (*E*)-enyne **1e** with allylzirconium **4** followed by desilylation (eq. 5), two spots were detected on TLC (R_f 0.57 and 0.54, hexane/EtOAc = 7/3). Careful chromatography (SiO_2) enabled their separation, and the less polar one proved to be the branched product (*E*)-**11** (52%). The more polar fraction (28%) was composed of two isomeric linear products, the expectable (6*E*, 8*E*)-**12** and, notably, a minor amount of the (6*Z*, 8*Z*)-**12**.[11] Interestingly, in the latter minor isomer the olefinic geometries were opposite to the former at two positions, the newly formed C(6)–C(7) double bond and also the C(8)–C(9) double bond embedded in the starting enyne. A similar situation was also the case for the corresponding (*Z*)-enyne **1f**; the regioselectivity was even poorer (eq. 6), where again the expectable linear product (6*E*, 8*Z*)-**12** was accompanied by its doubly-flipped geometrical isomer (6*Z*, 8*E*)-**12**.



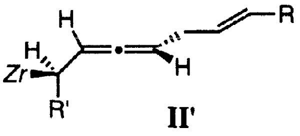
Unexpected formation of the "doubly-flipped" geometrical isomers in eqs. 5 and 6, although formed in small amounts, is intriguing, thereby suggesting any specific/selective nature of the side reaction. A plausible explanation involves the isomerization of the "terminal" allylmetallation product *via* 1,3-metallotropic shift.[12,13] In the reaction of (*E*)-enyne **1e**, for example, the vinylzirconium **I**, formed as an intermediate leading to the triene **12**, could isomerize to the doubly flipped isomer **III** *via* three events; 1,3-shift (*supra*; **I** → **II**) followed by C–C bond rotation (**II** → **II'**) and another 1,3-shift (*supra*; **II'** → **III**), which, upon hydrolysis, gives (6*Z*, 8*Z*)-**12**, isomeric to (6*E*, 8*E*)-**12** from the direct hydrolysis of **I**.[14]



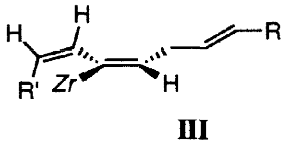
I



II



II'



III

In summary, the allylmetallation of conjugated enynes with allylzirconium occurs at the "yne" part of the enyne, where the regioselectivity depends critically on the steric demand of the substituent X.

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7. Modified MAO, hydrolysate of Me_3Al–*i*-Bu_3Al (2:1), Al = 6 wt% in toluene, $\bar{m}$w = 1200, used for this reaction was kindly donated from Tosoh Akzo Co.
8. When the reaction temperature was raised more slowly, the yield was lower. See ref. 1.
9. All new compounds were fully characterized by ^1H and ^{13}C NMR, IR, and high-resolution MS and/or combustion analysis.
10. The geometries of the double bonds in **5**, **7**, and **8** were confirmed by NOE correlation.
11. The silyl group was removed for facilitating the structural analysis. In the reaction of eq. 5, other two possible geometrical isomers, (6*Z*, 8*E*) and (6*E*, 8*Z*), were less than 2% in the linear product (HPLC). Conversely, the (6*E*, 8*E*) and (6*Z*, 8*Z*) isomers were <2% in the linear product **12** in the case of eq. 6.
12. For 1,3-metallotropic shift, see: a) Mashima, K.; Yasuda, H.; Asami, K.; Nakamura, A. *Chem. Lett.* **1983**, 219. b) Martin, H. A.; Lemaire, P. J.; Jellinek, F. *J. Organomet. Chem.* **1968**, *14*, 149. c) Mann, B. E. in *Comprehensive Organometallic Chemistry,* Wilkinson, G.; Gordon, F.; Stone, A.; Abel, E. W. Eds.; Pergamon: Oxford, 1982; Vol. 3, pp 89–172.
13. Though formally expectable, no allene-containing products were observed.
14. Note that the 1,3-shift (*supra*) of "*Zr*" to the other face of the C=C bond in **I** leads to *ent*-**II**, which also gives **III**.