Tetrahedron Letters, Vol. 34, No. 51, pp. 8301-8304, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Zirconium Catalyzed C-C Bond Formation Reaction of Conjugated Diynes with EtMgBr

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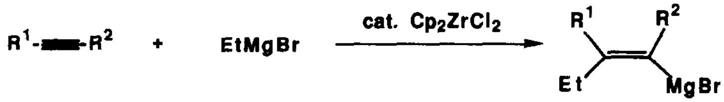
Abstract: The carbon-carbon bond formation reactions of diynes with EtMgBr can be catalyzed by Cp$_2$ZrCl$_2$. The final products, magnesiated enynes, readily undergo stereoisomerization to give a mixture of (E) and (Z) isomers. The stoichiometric reaction of diynes with ethylene zirconocene gives zirconacyclopentenes with alkynyl substituents in the α position with high regioselectivities.

Although zirconium catalyzed selective C-C bond formation reactions of alkenes with Grignard reagents such as ethylmagnesium bromide have been reported,[2] there are no precedents for alkynes to the best of our knowledge. In this paper we would like to report the first example of catalytic C-C bond formation of carbon-carbon triple bond with EtMgBr and also highly selective stoichiometric reaction of diynes with Cp$_2$ZrEt$_2$ or Cp$_2$ZrBu$_2$.

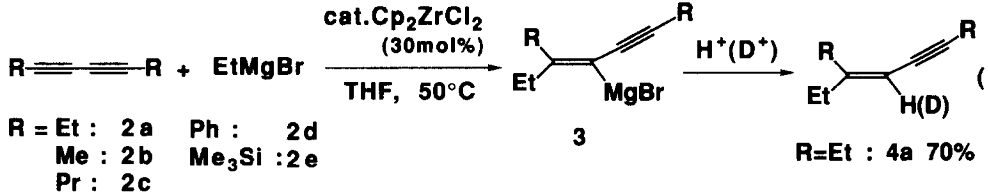


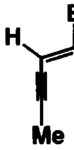
(1)

According to our mechanistic study on the catalytic reactions of alkenes with EtMgBr, the formation of ethylene-zirconocene and zirconacyclopentanes as intermediates, transmetalation with EtMgBr to open the zirconacyclopentane ring, and selective β-hydrogen abstraction are essential to the catalytic reaction of alkenes with EtMgBr.[2,3] Usually, alkynes dimerize easily on reduced zirconium to produce stable zirconacyclopentadienes even in the catalytic system Cp$_2$ZrCl$_2$/EtMgBr. As we already reported, a stoichiometric reaction of alkynes with Cp$_2$ZrEt$_2$ gave zirconacyclopentenes.[4] At low temperatures (0°C) these zirconacyclopentenes were inert toward transmetalation reaction with EtMgBr. At higher temperatures a second alkyne easily displaces the ethylene moiety of zirconacyclopentenes to afford zirconacyclopentadienes. This tendency of alkynes to form dimers on zirconium has been major problems for developing catalytic reactions of alkynes with EtMgBr.

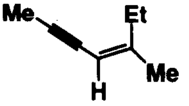
During the course of our study on a stoichiometric reaction of conjugated diynes with Cp$_2$ZrEt$_2$, we have found that a highly regioselective reaction of diynes with Cp$_2$Zr(CH$_2$=CH$_2$) takes place as described below and that some diynes do not dimerize at 50°C on reduced zirconocenes. These findings prompted us to develop the first example of zirconium catalyzed C-C bond formation reactions of C-C triple bonds, specifically that of diynes with EtMgBr.

In the presence of a catalytic amount of Cp_2ZrCl_2 (0.3 mmol, 0.088 g), 3,5-octadiyne **2a** (1.0 mmol, 0.106 g) reacted with EtMgBr (5.0 mmol, THF solution) at 50°C for 6h to give **4a** in 70% yield based on **2a** after hydrolysis. At 0°C or room temperature the reaction did not proceed catalytically, but the expected products were obtained under the stoichiometric conditions. At 50°C the diyne was completely consumed. Although analysis by GC showed that this reaction cleanly gave a single product, the product **3a** gradually decreased under the condition used here. Deuterolysis gave a monodeuterated derivative of **4a**. Carbon-carbon bond formation occurred at the C-1 carbon, and a carbon-magnesium bond was formed at the C-2 carbon of the diyne moiety as shown in eq 2. The regioisomeric purity of this product was very high (>99%). In the case of 2,4-hexadiyne **2b** or 4,6-decadiyne **2c**, the product was a mixture of **4b** and **4b'**(1h: yield 52%, ratio of **4b**:**4b'** = 67:33) or **4c** and **4c'**(6h; yield 63 %, ratio of **4c**:**4c'** = 57:43). Diynes **2d**-**2e** were completely consumed under catalytic conditions. However, the desired catalytic reaction products were not obtained.

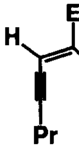




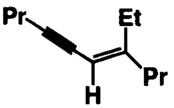
4b



4b'



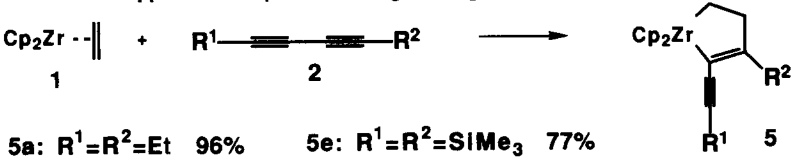
4c



4c'

A zirconium catalyzed carbometalation reaction of alkynes with $AlMe_3$ has been reported.[5] With some diynes, such as bis(trimethylsilyl)diyne, this reaction places the Me group at the C-2 carbon of diynes.[6] Thus, the regiochemistry of C-C bond formation in the $Cp_2ZrCl_2/AlMe_3$ reaction is different from that in the Cp_2ZrCl_2/EtMgBr reaction.

This regioselectivity of the C-C bond formation reaction of 3,5-octadiyne **2a** was clearly explained by the following stoichiometric reaction. When **2a** reacted with $Cp_2Zr(CH_2{=}CH_2)$ (**1**) which was in situ produced from Cp_2ZrCl_2 and EtMgBr, **5a** in which the alkynyl substituent was in the α position was formed in 96% yield. It is noteworthy that the zirconacyclopentene compounds **5** did not react with a second molecule of a diyne even at higher temperatures. The alkynyl substituent in the α position must stabilize **5** as observed with a Si group and Ph group as well. The ^{13}C NMR spectra of **5** showed that one of the alkynyl carbon signals appeared at about 140 ppm in the sp^2 carbon region, e.g. 144.20 ($R^1{=}R^2{=}Et$), 143.12 ($R^1{=}R^2{=}Pr$),

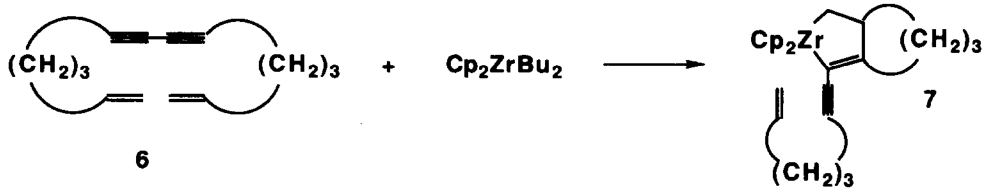


(3)

5a: $R^1{=}R^2{=}Et$ 96%
5b: $R^1{=}R^2{=}CH_3$ 98%
5c: $R^1{=}R^2{=}Pr$ 86%
5d: $R^1{=}R^2{=}Ph$ 87%
5e: $R^1{=}R^2{=}SiMe_3$ 77%
5f: $R^1{=}Ph$, $R^2{=}Bu$ 76%
(with **5f'**: $R^1{=}Bu$, $R^2{=}Ph$ 22%)
5g: $R^1{=}t\text{-}Bu$, $R^2{=}Ph$ 86%

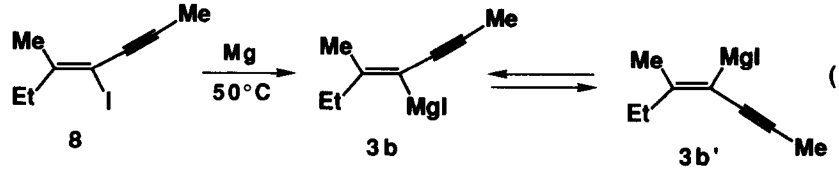
138.22 (R^1= t-Bu, R^2=Ph). These low field shifts most likely are due to interaction with Cp_2Zr moiety. The other alkynyl carbon signals appeared in the normal region of *sp*-carbon, e.g. 88.19 (R^1=R^2=Et), 87.53 (R^1=R^2=Pr) and 89.99 (R^1=t-Bu, R^2=Ph).

In the case of 1,13-tetradecadien-6,8-diyne (**6**) the bicyclization reaction cleanly took place using 1 equiv of Cp_2ZrBu_2 as shown below.



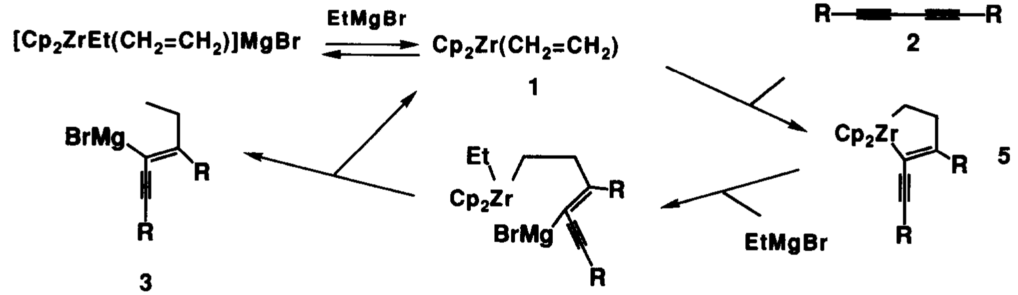
(4)

The stereochemistry of the double bond in the hydrolysis product derived from **5** is also noteworthy. In each case hydrolysis gave only one stereoisomer in which Et and H are cis to each other. On the other hand, the catalytic C-C bond formation reaction of 2,4-hexadiyne (**2b**) or 4,6-decadiyne (**2c**) afforded a mixture of stereoisomers. In order to understand this, the following reaction was carried out. Treatment of **8** with magnesium metal gave a mixture of **3b** and **3b'** at 50°C. After hydrolysis the ratio of **4b** and **4b'** was 57:43 (combined yield, 86%). This type of configurational isomerization of alkenyl metals is known for metalated vinylsilanes[7], metalated styrenes[8], and others.[9] However, stereoisomerization of metalated enynes appears to be unprecedented.



(5)

A plausible catalytic reaction mechanism is shown below. A similar mechanism to that for alkenes can be used for the catalytic C-C bond formation reaction of diynes using the Cp_2ZrCl_2/EtMgBr system. Zirconocene-ethylene, $Cp_2Zr(CH_2{=}CH_2)$ (**1**), is produced from Cp_2ZrCl_2 and 2 equiv of EtMgBr. This is stabilized as an ate complex $[Cp_2ZrEt(CH_2{=}CH_2)]MgBr$ under catalytic conditions.[3g] The ethylene complex **1** reacts with diyne **2** to give zirconacyclopentenes **5** as demonstrated by the stoichiometric reactions. Transmetalation between zirconacyclopentene and EtMgBr to open the ring is followed by β-H abstraction to give the magnesiated enyne **3** and **1**. The compound **3** is configurationally unstable. Its isomerization gives a mixture of (E) and (Z) isomers.



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(Received in Japan 27 July 1993; accepted 22 September 1993)