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Facile Cleavage of the Cβ-Cβ' Bond of Zirconacyclopentenes. Convenient Method for Selectively Coupling Alkynes with Alkynes, Nitriles, and Aldehydes

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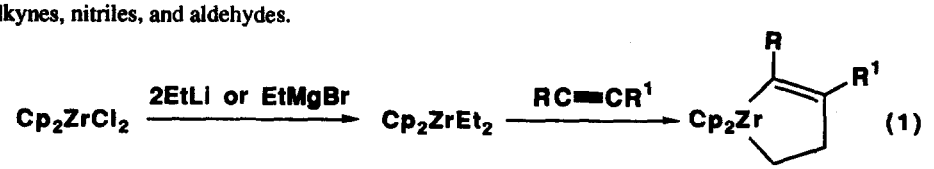
Abstract: The reaction of zirconacyclopentenes (1) with alkynes, nitriles, and aldehydes proceeds via cleavage of the Cβ-Cβ' bond of 1 and displacement of ethylene by the donors to give the corresponding five-membered zirconacycles, providing a convenient means of selectively coupling alkynes with π-donor compounds.

The reaction of alkynes with diethylzirconocene, generated *in situ* by treatment of Cp_2ZrCl_2 with 2 equivalents of ethylmagnesium halides or ethyllithium, can selectively produce the corresponding zirconacyclopentenes (1) in good yields (eq 1). Interestingly, zirconacyclopentenes (1) react at room temperature with various π-donors to give selectively the corresponding five-membered zirconacycles(2-4),while their reaction with a phosphine gives zirconocene-alkyne-phosphine complexes (5) (Scheme 1). The facile cleavage of the Cβ-Cβ' bond of zirconacyclopentenes[3,4] is analogous to that of zirconacyclopentanes.[5] It is, however, in striking contrast with the inertness of zirconacyclopentadienes which do not react with any of the reagents mentioned above under comparable conditions.[6] The known procedures[7-9] for the synthesis of 2-4 mostly require preformed Cp_2Zr-alkyne-phosphine complexes containing costly phosphines, e.g., PMe_3 and PPh_2Me, and/or cumbersome preparation of $Cp_2Zr(H)Cl$ for hydrozirconation of alkynes.[10,11] Consequently, the Cβ-Cβ' bond cleavage route herein reported offers a convenient alternative for selectively coupling alkynes with alkynes, nitriles, and aldehydes.



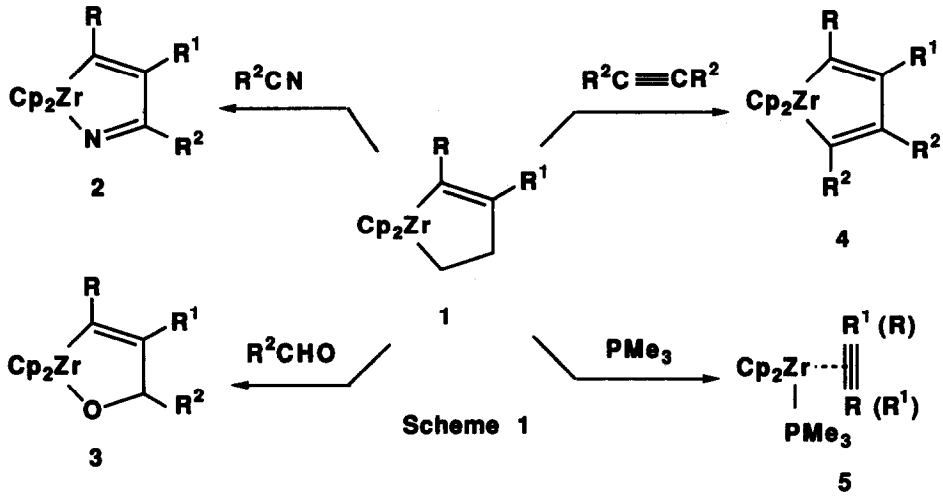
(1)

1

1a (80-90%, R = R¹ = *n*-Pr) **1b (87%, R = R¹ = Et)**

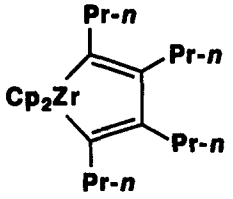
1c (87%, R = R¹ = Ph) **1d (84%, R = Ph, R¹ = Me)**

1e (74-87%, R = H, R¹ = *n*-Hex) **1f (40%, R = Me_3Si, R¹ = H)**

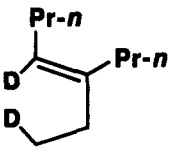


Scheme 1

Typically, treatment of Cp_2ZrCl_2 with 2 equivalents of EtMgBr in THF at -78°C for 1h followed by addition of 1 equivalent of 4-octyne and warming the reaction mixture to 0°C for 3h produced **1a** in 80-90% yields by analysis of ^1H NMR Cp signals. Other Cp_2Zr derivatives, one of which was identified as **4a** (R = R^1 = R^2 = Pr-n), were present in trace amounts. The identity of **1a** was established by (a) deuterolysis with DCl in D_2O to give a 73% yield of **6** with >98% D incorporation, (b) iodinolysis with I_2 to give **7** in 58% yield, and (c) carbonylation-iodinolysis to give **8** in 58% yield.[12] All of the yields of these organic products are isolated yields based on 4-octyne. This selective formation of zirconacyclopentenes proceeded at 0 °C even in the presence of 2 equivalents of 4-octyne. The desired product **1a** was formed in 80% yield and 0.99 equivalent of 4-octyne remained unreacted. The amount of **4a** was less than 5%. In marked contrast, the corresponding reaction of Cp_2ZrBu_2 with 4-octyne (1 equivalent) produced **4a** (97% of the maximum possible amount based on 4-octyne; 48% based on Zr) and **9**[12](24% based on Zr) as the major products along with only 3% yield of **10**. With 2 equivalent of 4-octyne, it is known that a quantitative yield of **4a** is produced from Cp_2ZrBu_2. It is likely that, in the reaction of Et_2ZrCp_2 with 4-octyne, Cp_2Zr-ethylene generated in situ must react with 4-octyne to give **1a** without undergoing extensively displacement of ethylene by 4-octyne, whereas displacement of 1-butene by 4-octyne to generate Cp_2Zr-4-octyne (**11**) must extensively take place in the corresponding reaction of Cp_2ZrBu_2. Once **11** is generated in the presence of 4-octyne, it would preferentially be converted to **4a**. The reaction of $Cp_2Zr(CH_2CH_2Ph)_2$ with 4-octyne falls between the two extremes mentioned above but more closely resembles the case of Cp_2ZrEt_2. Thus, it provided **12** and **4a** in 52 and 16% yields, respectively. Several additional zirconacyclopentenes represented by **1** have also been prepared in the yields indicated in eq 1. It is noteworthy that **1d**[13] and **1f** were obtained as 95% and 99% regioisomerically pure compounds, respectively. In the case of **1e**, the initial product obtained in 93% yield after 3h at 25°C was a 60:40 mixture of **1e** and its regioisomer. Upon standing at 25°C for 1-2 days either in the absence of any added reagents or in the presence of PMe_3, $PMePh_2$, or (E)-stilbene to stabilize a presumed intermediate Cp_2Zr-1-octyne similar to **11**, the regioisomeric purity of **1e** was improved to 85-90%,[3a] even though the overall yield somewhat decreased to 74-87%. We may now conclude that, even though the scope of the above-described procedure for selective synthesis of zirconacyclopentenes is practically limited to those cases where ethylene is the alkene component, i.e., preparation of **1**, its scope with respect to alkynes appears to be broad.



4a



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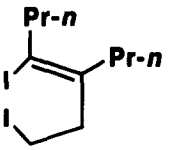

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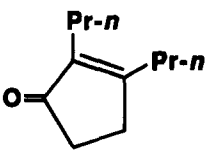

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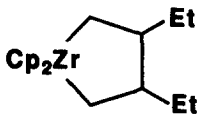

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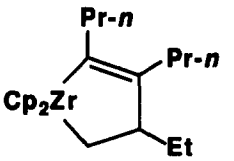

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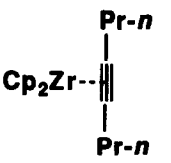

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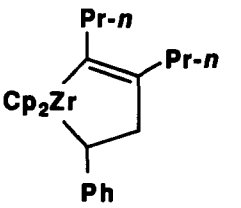

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The crucial finding of this study is that zirconacyclopentenes (1) derived from Cp_2ZrEt_2 and alkynes readily undergo cleavage of the C_β-$C_{\beta'}$ bond with extrusion of ethylene, thereby serving as convenient sources of Cp_2Zr-alkyne complexes. Specifically, the reaction of **1a** with 1 equivalent of MeCN at 25°C for 3h led to the formation of a 65% NMR yield of **2a** (R = R^1 = Pr-*n*, R^2 = Me, δ 5.76 assigned to Cp protons). A few other minor byproducts including **4a** (2%, δ 6.11) were present along with **1a** (4%). Protonolysis of the mixture provided (E)-3-(n-propyl)-3-hepten-2-one as a >99% isomerically pure species in 60% yield based on 4-octyne. Similarly, the reaction of **1a** with 1 equivalent each of benzaldehyde and heptaldehyde at 50°C for 3 h gave **3a** (R = R^1 = Pr-*n*, R^2 = Ph) and **3b** (R = R^1 = Pr-*n*, R^2 = Hex-*n*) in 65 and 52% NMR yields, respectively. A few other minor byproducts including **4a** (<5%) were present. Conversion of **3** into organic compounds via protonolysis is well documented.[8] The reaction of **1a** with 1 equivalent of 3-hexyne at 50°C for 1h selectively produced **4b** (R = R^1 = Pr-*n*, R^2 = Et) in 81% yield. The amounts of **4a** and the other symmetrical zirconacyclopentadiene **4c** (R = R^1 = R^2 = Et) were 3-4 and 6%, respectively. It is noteworthy that the use of an excess (3 equivalents) of 3-hexyne led to virtually the same results. The results clearly indicate that the initially introduced alkyne, i.e., 4-octyne, remains complexed to Cp_2Zr throughout the reaction. Free 4-octyne may, however, be released from Cp_2Zr upon decomposition of **1a** or **11** via other paths, such as Cp_2Zr dimerization. It is therefore not surprising that, in the absence of any added reagent, **1a** slowly decomposed even at 25°C to give **4a** (70% of the maximum possible amount based on **1a** generated in 85% yield). Finally, decomposition of **1c** in the presence of 1.2 equivalent of PMe_3 provided **5c** (R = R^1 = Ph) in 61% yield.

The following procedure for 4-octyne-3-hexyne cross coupling reaction via zirconacyclopentenes is representative. To a solution of **1a** prepared in THF at 0°C as described above was added 1 equivalent of 3-hexyne. The mixture was warmed up to 50 °C and stirred for 1h. Cross coupling product **4b** was selectively formed in 81% yield along with small amounts of homo coupling products of 3-hexyne (6%) and 4-octyne (3%). The ^1H NMR spectrum of **4b** showed a singlet peak at 6.05 ppm assigned to Cp. Its ^{13}C NMR spectrum revealed clean 15 peaks at 191.03, 190.24, 134.07, 132.63, 109.99, 40.19, 30.89, 29.49, 24.98, 23.41, 21.49, 16.14, 15.33, 14.66, 14.29 ppm, which were consistent with **4b**. Protonolysis of **4b** thus

formed gave the corresponding diene in 76% yield along with small amounts of homo coupling products of 3-hexyne (6%) and 4-octyne (3%).

In conclusion, the results herein presented not only provide synthetically attractive procedures but also added to a growing body of data pointing to the chemical lability of the C_{β}-$C_{\beta'}$ bond of coordinatively unsaturated five-membered zirconacycles, which may be attributable to agostic interaction between the C_{β}-$C_{\beta'}$ bond and the Zr empty orbital analogous to that suggested for β-hydrogen abstraction of dialkylzirconocenes.[14]

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