

Cp₂ZrCl₂—Et₃Al Reagent System in the Homo-Coupling of Trimethylsilyl-Substituted Alkynes †

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Abstract: The reaction of homo-coupling of alkynes using zirconocene reagents is an important basis for the efficient synthesis of polymer, oligomers and macrocycles. The most widely used reagents include Negishi reagent (“Cp₂ZrBu₂”), Takahashi reagent (“Cp₂ZrEt₂”), and Rosenthal reagent (Cp₂Zr(py)TMSC≡CTMS). Despite detailed studies of the reaction of Et₃Al with Cp₂ZrCl₂, the resulting zirconocene complexes could not be successfully used for intramolecular coupling of alkynes. We found that the reaction of trimethylsilyl-substituted alkynes with 0.5 equivalents of Cp₂ZrCl₂, 1 equivalent of Et₃Al in toluene at room temperature for 18 h gives, after hydrolysis/deuterolysis or iodination, functionalized products of the homocoupling of silyl-substituted alkynes in good yield. Cp₂ZrCl₂—Et₃Al reagent system was used for the preparation of macrocyclic cyclophane from 4,4'-bis((trimethylsilyl)ethynyl)-1,1'-biphenyl. The first positive results open the way for the synthesis of macrocyclic polyene compounds through the combination of diyne molecules.

Keywords: alkynes; cyclometallation; cyclophane; homo-coupling; organoaluminums; zirconocene

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1. Introduction

The reaction of homo-coupling of alkynes using zirconocene reagents is an important basis for the efficient synthesis of polymer, oligomers and macrocycles [1]. It is generally accepted that the transformation takes place through the intermediate formation of “Cp₂Zr” species that can be generated by the interaction of Cp₂ZrCl₂ with alkali and alkaline earth metals, as well as with alkyl derivatives of metals. The most widely used reagents include Negishi reagent (“Cp₂ZrBu₂”) [2], Takahashi reagent (“Cp₂ZrEt₂”) [3], and Rosenthal reagent (Cp₂Zr(py)TMSC≡CTMS) [4]. Despite detailed studies of the reaction of Et₃Al with Cp₂ZrCl₂ [5–9], the resulting zirconocene complexes could not be successfully used for intramolecular coupling of alkynes. Negishi has demonstrated that the reaction of diphenylacetylene with Et₃Al in the presence of 10 mol% of Cp₂ZrCl₂ in benzene at 55 °C gave a mixture of substituted alkene and diene in a 1:1 ratio with a total yield of 90% [10]. However, the reaction with 5-decyne under similar conditions resulted in the formation of only 5-ethyl-5-decene. By replacing Et₃Al with Pr₃Al, it was possible to convert 5-decyne into tetrasubstituted 1,3-diene in 38% yield with simultaneous formation of reduction products in the amount of 63% [10]. Thus, attempts to develop a synthetically useful methodology for the coupling of alkynes using trialkylaluminums and Cp₂ZrCl₂ were unsuccessful. However, from our early observations of the alkyne cycloalumination reaction with Et₃Al in the presence of catalytic amounts of Cp₂ZrCl₂, we noticed that trimethylsilyl substituted 1-hexyne under the reaction conditions give 1,4-diene hydrocarbons as a by-product in up to 20% yield. This gave hope for the possibility of selecting the

optimal conditions for the implementation of the homo-coupling reaction of silicon containing alkynes. The importance of this transformation was due to the possibility of its use for the preparation of macrocyclic zirconacyclopentadiene compounds through the combination of diyne molecules of the TMS-C≡C-R-C≡C-TMS type.

2. Results and Discussion

It was found that the reaction of silyl-substituted alkynes with 1 equivalent of Cp₂ZrCl₂ and 2 equivalents of Et₃Al in toluene at 23 °C for 18 h after hydrolysis/deuterolysis or iodinolysis gives homo-coupling products **2–4** in good yield (Table 1). A remarkable feature of the reaction is the complete absence of products of cyclic carbometallation **5**. In the case of 1-alkyl-2-(trimethylsilyl)acetylenes, the reaction proceeds with a high regioselectivity to give 3,4-dialkyl substituted 1,4-bis(trimethylsilyl)buta-1,3-diene.

Table 1. The homocoupling of silyl-substituted alkynes by Cp₂ZrCl₂–Et₃Al reagent.

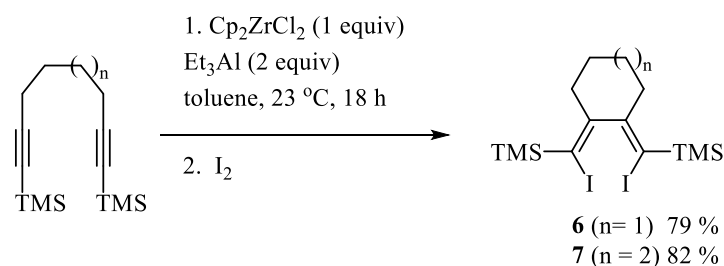
1. Cp₂ZrCl₂ (0.5 equiv)
Et₃Al (1 equiv)
toluene, 23 °C, 18 h
2. H₂O or D₂O or I₂

2 (X = H)
3 (X = D)
4 (X = I)

5 (X = D)

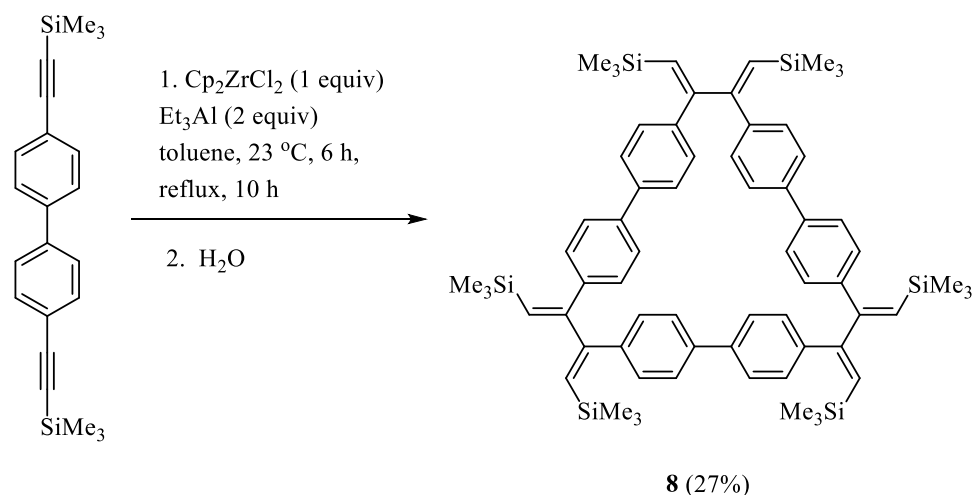
Entry	R	R'	X	 2 (X = H) 3 (X = D) 4 (X = I)	 5 (X = D)
1	Bu	TMS	H	86% (2a)	nd
2	Bu	TMS	I	88% (4a)	nd
3	Am	TMS	H	83% (2b)	nd
4	Am	TMS	D	85% (3b)	nd
5	Am	TMS	I	69% (4b)	nd
6	Bu	Bu	D	nd	82% (5c)
7	Bu	Ph	D	nd	69% (5d)

The reaction of trimethylsilyl-substituted α,ω -diynes (1,7-octadiyne, 1,8-nonadiyne) with Cp₂ZrCl₂–Et₃Al reagent after iodinolysis gives (1*Z*,2*Z*)-1,2-bis(iodo(trimethylsilyl)methylene)cycloalkanes **6** and **7** in good yield (Scheme 1). We were unable to obtain the products of the homo-coupling of alkynes in the case of 5-decyne and hex-1-yn-1-ylbenzene. As a result of the reaction, these alkynes gave after deuterolysis only products of cyclic carbometallation **5c** and **5d**. We failed to involve in the reaction acetylene derivatives of more sterically hindered silanes: hex-1-yn-1-yltriisopropylsilane, *tert*-butyl(hex-1-yn-1-yl)dimethylsilane and 1,2-bis(trimethylsilyl)ethyne. The above-mentioned acetylenic compounds were inert under the reaction conditions.



Scheme 1. The reaction of trimethylsilyl-substituted α,ω -diynes with $\text{Cp}_2\text{ZrCl}_2\text{—Et}_3\text{Al}$ reagent system.

The positive results opened the way for the synthesis of macrocyclic polyene compounds through the combination of diyne molecules. It is known that earlier the Negishi reagent was successfully used to obtain macrocyclic organozirconium compounds by homo-coupling of a number of organosilicon diynes [1]. Since the reagent we developed makes it possible to obtain products of the homo-coupling of silyl-substituted alkynes in good yield, we tried to involve organosilicon diyne in the reaction. It was found that the reaction of 4,4'-bis((trimethylsilyl)ethynyl)-1,1'-biphenyl with $\text{Cp}_2\text{ZrCl}_2\text{—Et}_3\text{Al}$ reagent system after hydrolysis gives macrocyclic cyclophane **8** in 27% yield (Scheme 2). Isolation of compound **8** was carried out by column chromatography. The relatively low yield of the product can be due to two circumstances: 1) the high Lewis acidity of Et_3Al promotes oligomerization and polymerization of the starting diyne; 2) in contrast to the previously published work [1], we failed to recrystallize the formed macrocyclic organometallic compound due to the presence of organoaluminum halides in the reaction mixture. The cyclophane **8** was characterised by ^1H and ^{13}C NMR spectroscopy. The trimeric structure was revealed by the MALDI-TOF data.



Scheme 2. The synthesis of macrocyclic cyclophane **8**.

3. Conclusions

The method developed by us allows one to carry out the homo-coupling of silyl-substituted alkynes one preparative stage. $\text{Cp}_2\text{ZrCl}_2\text{—Et}_3\text{Al}$ reagent system was used for the preparation of macrocyclic cyclophane from 4,4'-bis((trimethylsilyl)ethynyl)-1,1'-biphenyl. The first positive results open the way for the synthesis of macrocyclic polyene compounds through the combination of diyne molecules.

4. Experimental Part

The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-500 (500 MHz) spectrometer in CDCl_3 , chemical shifts were reported relative to TMS. Mass spectra were obtained on a Shimadzu GCMS QP2010 Plus GC-MS instrument (capillary column SPB-5 of 30 m \times 0.25 mm, carrier gas—helium, from 40 to 300 $^\circ\text{C}$ at a rate 8 deg/min, temperature of vaporizer 280 $^\circ\text{C}$, ion source temperature 200 $^\circ\text{C}$, ionization energy 70 eV). Chromatographic analysis was carried out on a chromatograph Shimadzu GC-9A, GC-2014 [column of 2 m \times 3 mm, stationary phase silicone SE-30 (5%) on Chromaton N-AW-HMDS, from 50 to 270 $^\circ\text{C}$, heating rate 8 deg/min, carrier gas—helium (47 mL/min)].

4.1. Homo-Coupling of Trimethylsilyl-Substituted Alkynes by $Cp_2ZrCl_2-Et_3Al$ Reagent

A suspension of Cp_2ZrCl_2 (292 mg, 1 mmol) in 3 mL of toluene in a 25 mL round bottom flask was cooled with an ice-bath and then Et_3Al (0.3 mL, 2 mmol) was added. After stirring the mixture at 0 °C for 30 min, 1 mmol of trimethylsilyl-substituted alkyne or 0.5 mmol of trimethylsilyl-substituted α,ω -diyne was added. The mixture was stirred at room temperature for 18 h. Then the mixture was diluted with 5 mL of hexane and 3 mL of H_2O (to prepare **2a,b**) or 3 mL of D_2O (to prepare **3b**) was added dropwise while cooling the reactor flask with an ice-bath. The precipitate was filtered on a filter paper. To prepare the compounds **4a, 4b**, a solution of I_2 (254 mg, 2 mmol) in 5 mL of THF was added to the reaction mixture while cooling the reactor flask with an ice-bath and stirred at room temperature for 1 h. To prepare the compounds **6, 7**, a solution of I_2 (254 mg, 2 mmol) in 5 mL of THF was used. The aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous $CaCl_2$. Evaporation of solvent and purification of the residue by column chromatography (hexane/ethyl acetate, 5:1) gave a colourless oil.

((1*E*,3*E*)-2,3-dibutylbuta-1,3-diene-1,4-diyl)bis(trimethylsilane) (**2a**)

Yield: 133 mg (86%); $R_f = 0.8$ (hexane/ethyl acetate, 5:1). 1H NMR (500MHz, $CDCl_3$): $\delta = 0.14$ (s, 9H, C(7)H₃), 0.92 (t, $J = 7$ Hz, 3H, C(6)H₃), 1.28–1.36 (m, 4H, C(4, 5)H₂), 2.29 (t, $J = 7$ Hz, 2H, C(3)H₂), 5.48 (s, 1H, C(1)H). ^{13}C NMR (500MHz, $CDCl_3$): $\delta = 0.36$ (C(7)), 14.06 (C(6)), 22.93 (C(5)), 31.69 (C(4)), 33.74 (C(3)), 125.07 (C(1)), 160.67 (C(2)). MS (EI): m/z , % = 311 (3) [M⁺], 295 (5), 268 (9), 237 (15), 207 (10), 165 (7), 138 (6), 73 (100), 45 (9).

4.2. Homo-Coupling of 4,4'-Bis(trimethylsilyl)ethynyl-1,1'-biphenyl by $Cp_2ZrCl_2-Et_3Al$ Reagent

A suspension of Cp_2ZrCl_2 (584 mg, 2 mmol) in 10 mL of toluene in a 50 mL round bottom flask was cooled with an ice-bath and then Et_3Al (0.6 mL, 4 mmol) was added. After stirring the mixture at 0 °C for 30 min, 4,4'-bis(trimethylsilyl)ethynyl-1,1'-biphenyl (346 mg, 1 mmol) was added. The mixture was stirred at room temperature for 6 h. Then the mixture was refluxed for 10 h. diluted with 5 mL of hexane and 3 mL of H_2O was added dropwise while cooling the reactor flask with an ice-bath. The precipitate was filtered on a filter paper and transferred into 100 mL round bottom flask with 50 mL of THF. Then trifluoroacetic acid (3.8 mL, 50 mmol) was added to a solution and the mixture was stirred for 3 h. Evaporation of solvent and purification of the residue by column chromatography (SiO_2 , hexane/ $CHCl_3$ 5:1) gave a colorless solid (94 mg, 27%). 1H NMR (500MHz, $CDCl_3$): $\delta = -0.11$ (s, 18H), 6.44 (br.s, 6H), 7.35–7.9 (m, 24H). ^{13}C NMR (500MHz, $CDCl_3$): $\delta = -0.3$, 119.2, 127.8, 131.5, 141.0, 147.2, 159.1.

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