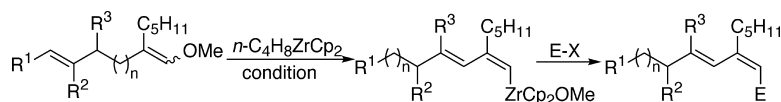Article

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Stereoselective Preparation of Dienyl Zirconocene Complexes via a Tandem Allylic C−H Bond Activation-Elimination Sequence

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Abstract: Several dienyl zirconocene derivatives were easily prepared, as unique geometrical isomers, from simple non-conjugated unsaturated enol ethers with (1-butene)ZrCp$_2$ complexes. This new methodology is based on a tandem allylic C-H bond activation-elimination sequence and the mechanism has been mapped out by deuterium labeling experiments. The stereochemical outcome of this process was determined by addition of several electrophiles. Moreover, when the organometallic derivative is vinylic as well as allylic such as in **44−47Zr**, an unexpected reversal of the stereochemistry has been found during the zirconium to copper transmetalation step.

Introduction

The intermolecular addition of organometallics **1** to alkynes **2** (carbometalation)[1] constitutes an excellent method for the preparation of alkenyl organometallics of type **3**, which after a reaction with electrophile reagents (E−X) provide polysubstituted olefins (Scheme 1).

In particular, carbocupration,[1e] zirconium-catalyzed carboalumination,[2] nickel-catalyzed carbozincation,[3] allylmetalation of metalated alkynes,[3] allylzirconation,[5] allylgallation,[6] allylmanganation,[7] and alkyllithiation[8] have high synthetic potential due to wide applicability. The addition of different substituted allyl- and propargylsilanes to unactivated alkynes in the presence of catalytic amounts of Lewis Acids was also recently reported.[9]

Although dienylmetals could be very useful synthetic precursors for various targets, the vinylmetalation of alkynes has

**Scheme 1.** General Scheme for Intermolecular Carbometalation Reaction of Alkynes
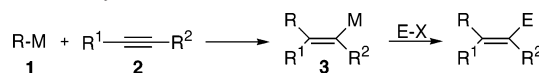
remained comparatively unexplored.[1,10] The principal reason for this lack of development is that the vinylmetalation of unactivated alkyne **2** with **1** (R = alkenyl) affords a new vinylic organometallic derivative **3**, which has a similar reactivity to that of **1** and therefore can participate also in a subsequent carbometalation reaction. In this case, an oligomerization of the unsaturated substrates results.

In the past decade, reactions based on dialkylzirconocene complexes have found tremendous evolution.[11] These achievements have triggered an avalanche of interest and many elegant applications described in the literature corroborate the notion that zirconocene-based synthesis of complex targets may clearly outperform more conventional approaches.[12] Particularly in the field of metalated dienes, zirconocene derivatives were already successfully used and some of the more important examples will be briefly described.

Vinylmetalation of alkynes can be performed in a two-step procedure (Scheme 2): stereoselective preparation of zironacyclopentadiene derivative **4** followed by the stereoselective reaction of **4** with an electrophile to give the carbometalated dienyl product **5**. The coupling of two alkynes, via low-valent zirconocene species leads to the formation of zirconacyclopen-

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Scheme 2. Preparation of Zirconadienyl Complexes
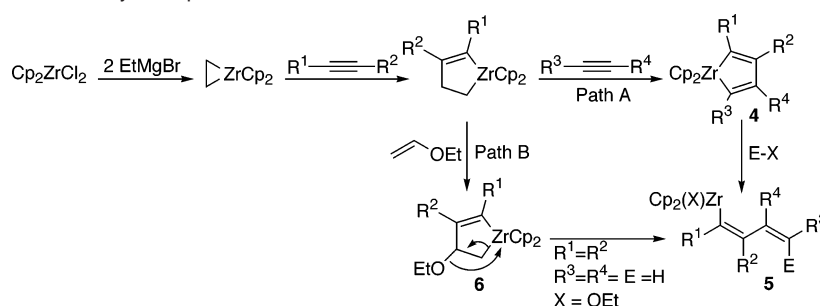
Scheme 3. Insertion of 1-chloro-1-lithioalkenes into Organozirconocenes
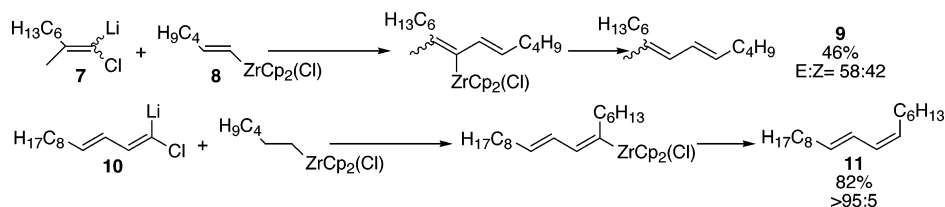
tadiene complexes.[13] For the preparation of unsymmetrical zirconacyclopentadienes, Cp_2ZrEt_2 as well as Cp_2ZrBu_2 (Negishi reagent) under ethylene gas were found to be very useful reagents but the regiochemistry for each alkyne is controlled by the nature of the substituents. With a trimethylsilyl-substituted acetylene (R^1 or R^3 = $SiMe_3$, R^2 or R^4 = alkyl), the trimethylsilyl groups are placed in α-positions of zirconacyclopentadienes with excellent selectivity.[14] With a phenyl-substituted alkyne (R^1 or R^3 = C_6H_5, R^2 or R^4 = alkyl), regioselective reactions are usually observed, although in some cases a mixture of two isomers may be formed. However, if two π-compounds are similar in chemical properties such as in 2-pentyne (R^1 or R^3 = Me, R^2 or R^4 = Et), nonselective cyclization should be expected in the formation of the corresponding zirconacyclopentadiene **4** and therefore nonselective formation of metalated diene **5** will result (Scheme 2).

Indeed, even if **4** is obtained regiospecifically, the preparation of stereodefined metalated dienyl zirconocenes requires a stereospecific reaction of only one carbon−zirconium bond (either C(R^1)−Zr or C(R^3)−Zr) of **4** with electrophiles (Scheme 2, path A). Consequently, only very few examples were reported for the stereoselective reaction of unsymmetrical zirconacyclopentadienes with electrophiles and they are all related to starting materials in which the nature of R^1 and R^3 are very different such as 2,3-diphenyl 4,5 dialkylzirconacyclopentadienes (R^1 and R^2 = alkyl, R^3 and R^4 = phenyl).[15] Ethenylzirconation reaction has been also reported by combination of Cp_2ZrEt_2 with vinyl ethers (Scheme 2, path B). In such a case, the elimination of the alkoxy group in the zirconacyclopentene intermediate **6** generates the dienyl system **5**.[16] However, although with symmetrical internal alkynes such as 5-decyne and diphenylacetylene, vinylzirconation products were obtained with a good isomeric purity, unsymmetrical alkynes such as 1-propynyl benzene (R^1 = Ph, R^2 = Me) gave a mixture of isomers in an 81:19 ratio.

Hydrozirconation of alkynes followed by insertion of 1-halo-1-lithio-alkenes, generated in situ by lithium tetramethylpiperidide deprotonations of vinyl halides, affords dienyl zirconocene species, which may be further functionalized.[17] When the insertion of the carbenoid derived from the deprotonation of (*E*)-1-chloro-2-methyl-1-octene **7** into (*E*)-1-hexenylzirconocene

Scheme 4. Transformation of 2-Silyloxy-1,3-diene into 1-Methylene-2-propenylzirconium Derivatives
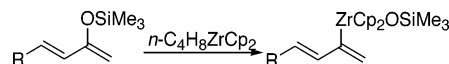
chloride **8** is performed at low temperature, the expected product **9** is obtained in moderate yield and isomeric ratio.[18] However, the deprotonations and insertion of (*E,E*)-4-alkyl-1-chloro-1,3-butadiene **10** with alkylzirconocene chloride followed by hydrolysis gave the nonterminal diene with high yield and stereoselectivity (Scheme 3).

The same methodology was recently used for the geminal dimetalation of alkylidene carbenoids with silylboranes and diborons.[19]

Finally, Jan Szymoniak and co-workers have reported that 2-silyloxy-1,3-diene reacts with zirconocene Cp_2Zr(1-butene) to give 1-methylene-2-propenylzirconium compounds which have been used as 2-dienylation reagents by addition of several electrophiles (Scheme 4).[20]

The impressive results summarized above are perhaps the most compelling examples of the power of zirconocene compounds in organic synthesis but in a general sense, are also illustrative for the serious limitations of the methodologies for the stereoselective preparation of dienyl zirconocene derivatives:

(1) R^1 and R^2 as well as R^3 and R^4 in **4** have to be of different electronic nature (Scheme 2, path A)

(2) Only unsubstituted terminal double bond can be prepared by using the strategy described in Scheme 2, path B (**6** to **5**)

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Scheme 5. Isomerization Reaction of Dienes (path A) Combined with the Preparation of Vinylic Organometallic Derivatives (path B) as a New Source of Metalated Dienyl Zirconocenes Complexes (path C)
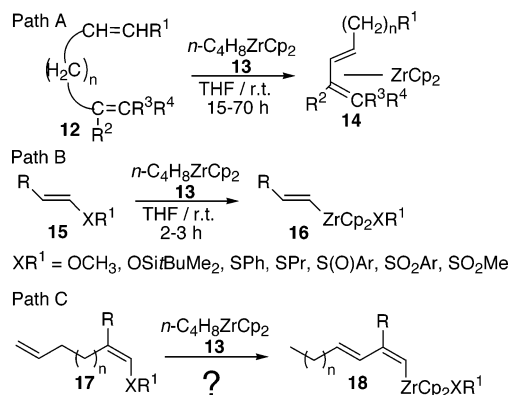
(3) Problems of stereoselectivity arise when unstable carbenoids have to be used (except in the methodology leading to **11**, Scheme 3)

(4) Stereoselectivity of the reaction could not be addressed in the preparation of 1-methylene-2-propenylzirconium (Scheme 4).

On the other hand, the transition metal catalyzed isomerization of terminal olefins into internal olefins has been extensively studied and in general a mixture of 1-alkenes, (*E*)- and (*Z*)-2-alkenes, reflecting the thermodynamic equilibrium, is obtained.[21] Some low-valent titanocene derivatives are highly effective and stereoselective in favor of the (*E*)-2-isomer.[22] When nonconjugated dienes such as **12** containing one or two substituted vinyl groups are treated with the zirconocene **13** (easily prepared from commercially available Cp_2ZrCl_2 and 2 equivalents of *n*-BuLi and called Negishi reagent),[11] a regioisomerization of the less-substituted double bond can occur and lead to the formation of the conjugated diene-zirconocene complexes **14** (Scheme 5, path A).[23] As we have recently developed a new and straightforward stereoselective preparation of vinylic organometallic derivatives **16** from heterosubstituted alkenes **15** such as vinyl enol ethers,[24] silyl enol ether,[24] vinyl (alkyl or aryl) sulfides, vinyl sulfoxides and even vinyl sulfones,[25] in a one-pot procedure (Scheme 5, path B), we though that the combination of the isomerization process with the elimination reaction would lead to an efficient preparation of stereodefined metalated zirconocene complexes **18** from simple unsaturated enol ether **17** (Scheme 5, path C). Indeed, all of these heterosubstituted alkenes **15**[26] smoothly react with the same Negishi reagent (1-butene)$ZrCp_2$ **13** that was used for the isomerization reaction of **12**.

Results and Discussion

All of our starting materials were very easily prepared in a single-pot operation by treatment of the alkoxy-allene[27] **19** with lithium organocuprate and trapping the resulting alkenyl copper

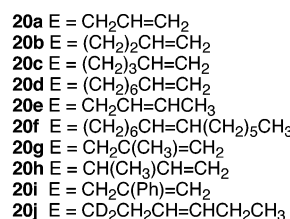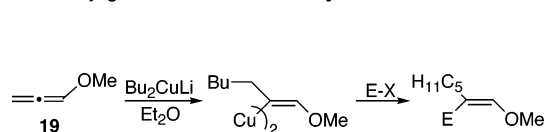**Scheme 6.** Preparation of Nonconjugated Enol Ether **20a**–**j**

20a E = $CH_2CH=CH_2$
20b E = $(CH_2)_2CH=CH_2$
20c E = $(CH_2)_3CH=CH_2$
20d E = $(CH_2)_6CH=CH_2$
20e E = $CH_2CH=CHCH_3$
20f E = $(CH_2)_6CH=CH(CH_2)_5CH_3$
20g E = $CH_2C(CH_3)=CH_2$
20h E = $CH(CH_3)CH=CH_2$
20i E = $CH_2C(Ph)=CH_2$
20j E = $CD_2CH_2CH=CHCH_2CH_3$

Table 1. Preparation of Isomerically Pure Dienes and Trienes

entry	comp	R^1	R^2	R^3	n	condition[a]	E–X	pdts	yield[b](%)
1	**20a–Z**	H	H	H	0	A	H_3O^+	**24**	80
2	**20a–Z**	H	H	H	0	B	H_3O^+	**24**	80
3	**20a–Z**	H	H	H	0	C	H_3O^+	**24**	80
4	**20a–Z**	H	H	H	0	A	I_2[c]	**25**	75
5	**20a–Z**	H	H	H	0	B	NBS[c]	**26**	60
6	**20a–Z**	H	H	H	0	A	NCS	**27**	60
7	**20a–Z**	H	H	H	0	A	AllylCl[d]	**28**	70
8	**20a–E**	H	H	H	0	A	AllylCl[d]	**28**	72
9	**20b**	H	H	H	1	A	AllylCl[d]	**29**	70
10	**20c**	H	H	H	2	A	AllylCl[d]	**30**	71
11	**20d**	H	H	H	5	A	AllylCl[d]	**31**	70
12	**20e**	CH_3	H	H	0	A	AllylCl[d]	**29**	80
13	**20f**	Hex	H	H	5	A	H_3O^+	**32**	61

[a] Condition A: THF, 15 min, +50 °C; condition B: Et_2O, 30 min, +35 °C; condition C: toluene, 15 min, +65 °C. [b]Isolated yield after purification by chromatography on silica gel. [c]Iodo- and bromodiene are unstable at room temperature and isomerized with time. [d]Obtained after a transmetalation step with 10 mol % of CuCl•2 LiCl.

with different unsaturated alkyl halides to give **20a**–**j** as reported by Normant and Alexakis (Scheme 6).[28]

Originally, **20a** was treated with (1-butene)$ZrCp_2$ **13** in THF at room temperature and the evolution of the reaction was followed by gas chromatography of hydrolyzed aliquots and by ^1H NMR of the reaction after hydrolysis. This examination indicated that the starting material was consumed within 12 h with concomitant formation of several products including the expected diene **24** as the major product (with a maximum 60% yield after hydrolysis, Scheme 7).

The ^1H spectrum of **23a** in C_6D_6/Et_2O solution showed two singlet peaks at 6.59 and 5.8 ppm assigned to the Zr–CH(sp^2) moiety and to the Cp protons respectively and a multiplet at 6.3 and 5.8 ppm for the hydrogens of the nonmetalated double bond. Its ^{13}C NMR spectrum revealed one singlet at 173.4 and 110 ppm which were assigned to the Zr–C(sp^2) moiety and Cp respectively and two more sp^2 carbons at 138.2 and 120.3 ppm.

On the other hand, when **20a** was treated with **13** either in THF at +50 °C for 15 min (condition A, Table 1), in Et_2O at +35 °C for 30 min (condition B, Table 1) or in toluene at +65 °C for 15 min (condition C, Table 1), the corresponding diene was constantly obtained with a yield of 80% (Scheme 7 and Table 1, entries 1 to 3).

Interestingly, only in the experiments that have been done at room temperature, the addition product **22** as well as dimers of **21** were detected and were attributed to the putative intermediate **21** (Scheme 7). Then, this zirconacycle intermediate disappears in favor of the dienyl zirconocene complex, likely via the formation of (alkene)zirconocene **23** through a skeletal rear-

Scheme 7. Tandem Isomerization–Elimination Sequence for the Preparation of Dienyl Zirconocenes Derivatives
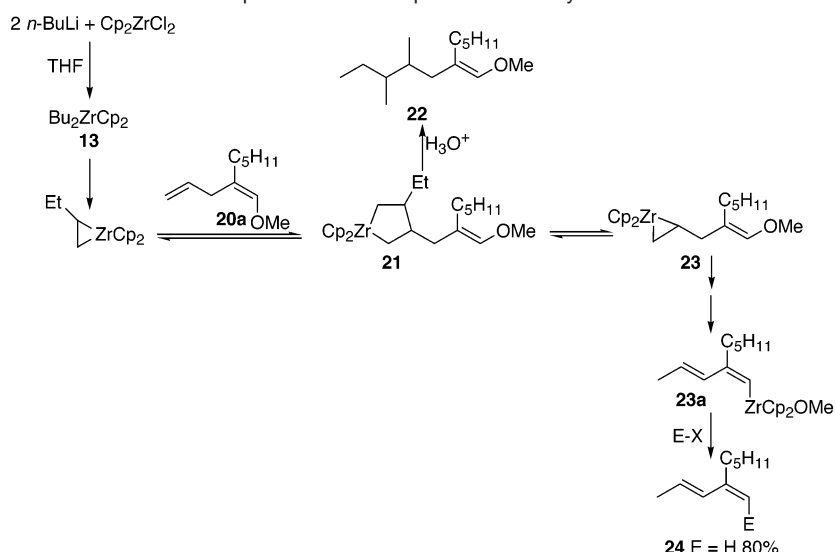
rangement[29] and then isomerization to lead to **24**. These results support an associative mechanism involving the intermediary formation of monocyclic zirconacyclopentane. When the reaction is performed at higher temperature (reflux of solvent), the equilibrium between **21** and **23** is very rapidly displaced in favor of **23**, which can cleanly undergo the isomerization process. The last experimental condition will be further generally used for the preparation of dienyl zirconocenes[30] (see scope of the reaction in Table 1).

The presence of a discrete organometallic species as well as the stereochemistry of the metalated diene were first checked by iodinolysis and bromolysis (entries 4 and 5, Table 1) but the corresponding iodo and bromo dienes **25** and **26** were found to be unstable and rapidly isomerized to a mixture of (*E*) and (*Z*)-isomers. Thus, to have a better picture of the stereochemical outcome of the process, we treated the crude reaction mixture with *N*-chlorosuccinimide (Table 1, entry 6) and the corresponding chloro diene **27** was isolated in 60% yield with a isomeric ratio >98/2. As alternative solution, we have also determined the stereochemistry of the reaction by addition of allyl chloride, in the presence of a catalytic amount of copper salt, to the dienyl zirconocene derivative (Table 1, entry 7).[31] **28** was obtained in good overall yield with an isomeric ratio greater than 98/2 in all cases. The (*E,Z*) stereochemistry of the 5-pentyl-octa-1, (4*Z*), (6*E*)-triene **28** was deduced on the basis

of differential Nuclear Overhauser effect spectra. When the same reaction was performed on the opposite isomer of the enol ether, namely the *E*-isomer (easily obtained from the carbocupration of alkoxy-allene but in THF as solvent instead of Et$_2$O, Scheme 6),[28] the same (*E,Z*)-dienylmetal was obtained as determined by the stereochemistry of the resulting product after reaction with allyl chloride (entry 8, Table 1). So, whatever the stereochemistry of the starting enol ether, a unique isomer of the dienyl zirconocene is obtained at the end of the process. Further on, a mixture of *E,Z*-isomers will be used as starting ω-ene-enol ether **20a**–**h**. The formation of dienyl zirconocenes is not limited to those dienes with a one-carbon tether (Table 1, entries 9 to11). Surprisingly, **20b**–**d** (with 2, 3 and 6 carbons tether respectively) also underwent this tandem reaction as fast as **20a** (only 15 min at +50 °C in THF) and in good overall yields. When the migrating double bond is 1,2-disubstituted such as in **20e** (Table 1, entry 12), our tandem sequence of isomerization-elimination still proceeds very efficiently and after transmetalation of the resulting dienyl zirconocene with copper salt, the allylation reaction gave the (*E,Z*)-triene **29** as unique isomer in 80% isolated yield. By combination of a long tether chain (6 carbons) with a 1,2-disubstituted olefin as in **20f**, diene **32** was isolated in 61% yield.

However, when the double bond is 1,1-disubstituted or if an alkyl group is located in the carbon tether such as in **20g** and **20h** respectively (Scheme 6), the reaction proceeds only in very low yield (<10%). The limitation of this new methodology could be attributed to an unfavorable initial ligand exchange between (1-butene)ZrCp$_2$ **13** and the migrating olefin for steric reason but also to the formation of a hypothetically less stable trisubstituted zirconacyclopropane, **33** or **34** which should be obtained after the first migration of the double bond (Figure 1). To overcome these limitations, the more bulky bis(trimethylsilyl)acetylene complex of zirconium **35** (Rosenthal's complex),[32] which has recently offered a number of compelling advantages in synthesis,[33] was tested in our reaction with **20g** with the hope that the release of the bulky bis(trimethylsilyl)-acetylene, after the ligand exchange, will be enough to drive

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Scheme 8. Mechanistic Hypothesis for the Tandem C−H Bond Allylic Activation−Elimination Sequence
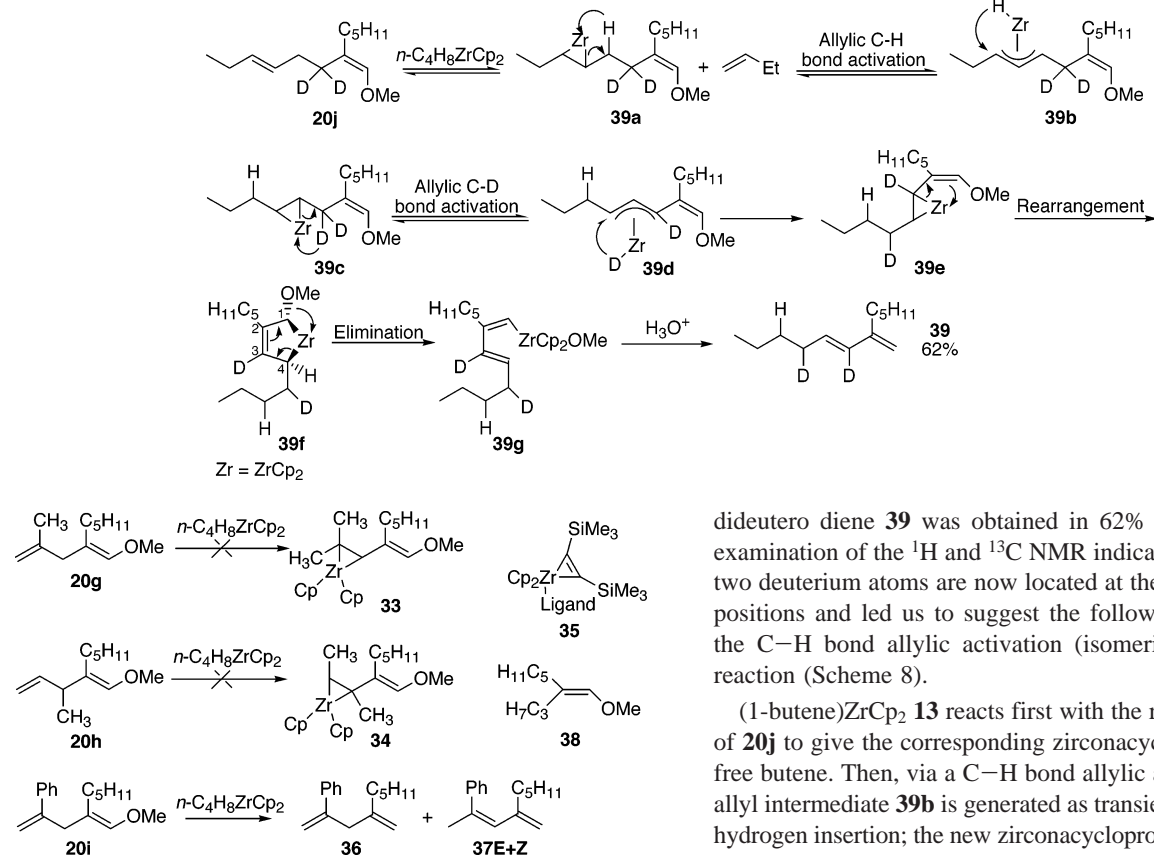
Figure 1. Limitation of the tandem isomerization-elimination sequence.

the reaction to completion. Unfortunately, no isomerization-elimination was observed. Therefore, the precursor of a potentially more stable trisubstituted zirconacyclopropane **20i** was prepared and submitted to the isomerization-elimination sequence. After hydrolysis, three products **36**/*Z*-**37**/*E*-**37** were obtained in a 2.3/3/1 ratio respectively; Thus, when the migrating 1,1-disubstituted double bond is slightly activated toward the formation of the zirconacyclopropane, the expected diene (beside the direct transformation of the methoxy enol ether into **36** after hydrolysis), could be formed but in this case, as a mixture of two geometrical isomers.

To have more insight on the reaction mechanism and on the stereochemical outcome of the reaction, we have performed the following two experiments: First, we have checked that the reaction of trisubstituted enol ether such as **38** did not lead to the vinylic organometallic derivative[24] (Figure 1) indicating that this tandem reaction should occur first by the isomerization of the remote double bond (only in the case of **20i**, the direct transformation of methoxy-enol ether into organometallic derivative was detected, most probably due to a template effect between the zirconocene **13** and the nonmigrating double bond); then, we have studied this isomerization reaction with deuterium labeling. Therefore, the dideutero enol ether **20j** was easily prepared by reaction of the alkoxy-allene **19** with dibutylcuprate followed by addition of the electrophile $CH_3CH_2CH=CHCH_2$-CD_2I, itself obtained by reduction of ethyl *trans*-3-hexenoate with $LiAlD_4$ and transformation of the primary alcohol into iodide. When **20j** was treated with 1.3 equivalent of (1-butene)-$ZrCp_2$ **13** in THF for 15 min at +50 °C, the corresponding 3,5-

dideutero diene **39** was obtained in 62% isolated yield. The examination of the ^{1}H and ^{13}C NMR indicates that, indeed, the two deuterium atoms are now located at the vinylic and allylic positions and led us to suggest the following mechanism for the C−H bond allylic activation (isomerization)-elimination reaction (Scheme 8).

(1-butene)$ZrCp_2$ **13** reacts first with the remote double bond of **20j** to give the corresponding zirconacyclopropane **39a** and free butene. Then, via a C−H bond allylic activation,[34] the η^3-allyl intermediate **39b** is generated as transient species and after hydrogen insertion; the new zirconacyclopropane **39c** is formed. By the same sequence, namely C−D bond allylic activation with deuterium migration (**39c** to η^3-allyl **39d** and then deuterium insertion), the zirconacyclopropane **39e** is produced. As soon as **39e** is formed, an irreversible step occurs transforming the zirconacyclopropane **39e** into zirconacyclopentene **39f**, which undergoes a β-elimination reaction to lead to **39g** and then **39** after hydrolysis. On the basis of this mechanism, we can easily understand that the stereochemistry of the starting enol ether has no effect on the stereochemistry of the dienyl zirconocene; the carbon-heteroatom bond of the metalated center in **39f** can freely epimerize to give the most stable isomer. Such an isomerization could be caused by an interaction between the ether moiety and the zirconium atom, which would weaken the C_1−Zr bond and facilitate the isomerization.[35] In the particular experiment described in Scheme 8, we did not see any scrambling of deuterium atoms along the carbon skeleton and this can be explained by the initial position of the two deuterium atoms. Indeed, in this C−D bond allylic activation step, as soon as the intermediate **39e** is formed, an irreversible rearrangement-elimination reaction (**39e** to **39g**) occurs and therefore drives the reaction toward the metalated diene **39g**. However, when the two-deuterium atoms are located in a different place in the tether, a scrambling of deuterium is observed along this tether.

The unique stereochemistry of the diene is therefore resulting from the elimination step and not from a further isomerization of the dienyl zirconocene with zirconocene derivatives (i.e., Cp_2-

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Scheme 9. Stereoselective Preparation of (2*E*, 4*Z*)-Decadiene
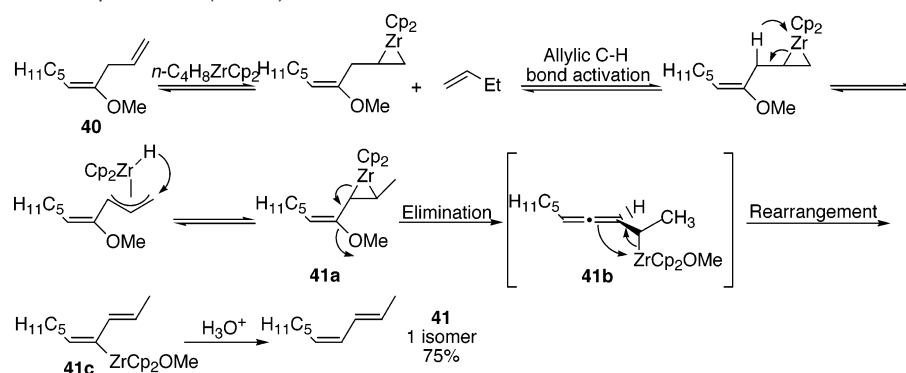
Zr-catalyzed stilbene stereoisomerization)[36] since the hydrozirconation reaction of several 1*E*-ene-3-yne and 1*Z*-ene-3-yne derivatives with Cp$_2$ZrH(Cl) lead only to the (*E*,*E*)- and (*Z*,*E*)-isomers respectively in good yields.[37]

In this new tandem allylic C—H bond activation followed by an elimination reaction, substituted 1-zircono-1*Z*,3*E*-dienes (zirconium moiety at the terminal position of the dienyl system) were easily prepared. With the idea to extend this methodology to the stereoselective synthesis of 3-zircono-1,3-diene (zirconium moiety at the internal position of the dienyl system), we have prepared and investigated the reactivity of **40** with (1-butene)-ZrCp$_2$ **13** (**40** was obtained by carbocupration of the α-allyl alkoxy-allene).[38] When **40** was submitted to the tandem reaction, the diene **41** was isolated after hydrolysis as a unique (*E*,*Z*)-isomer in 75% isolated yield (Scheme 9).

When the migrating group is geminated to the leaving group such as in **40**, the C—H bond allylic activation leads to **41a**, which subsequently undergoes now a β-elimination reaction to lead to the β-metalated allenyl intermediate **41b**. Then, **41b** is isomerized into its more stable dienyl form **41c**[39] in which the alkyl and the organometallic groups are anti to each other for steric reason. After hydrolysis, a unique isomer is observed (determined by NOE effects). Although this tandem reaction led also to the expected diene as unique isomer in good chemical yield, this methodology had a serious drawback from a preparative point of view because **40** could not be purified by column chromatography. Indeed, each time that we have tried to purify **40**, the ketone resulting from the hydrolysis of the enol ether moiety was obtained (enol ether from ketone is much less stable toward purification than enol ether from aldehyde). The isolated yield obtained for **41** is therefore based on the crude starting material **40** used without purification. This very promising route for the preparation of metalated diene such as **41c** associated with the problem of stability of α-substituted enol ether **40** led us to consider an alternative starting material. We consequently turned our attention to the preparation of sulfonyl 1,3-dienyls derivatives.[40] As for the enol ether methodology, the main advantage of this approach is the very easy preparation of acyclic 2-arylsulfonyl 1,3-dienes **42a**−**d** from allylic sulfones and aldehydes in a single-pot operation as described in Scheme 10.[41]

Scheme 10. Preparation of Acyclic 2-Arylsulfonyl 1,3-Dienes

42a R^1 = H, R^2 = Ph, 89%
42b R^1 = H, R^2 = *n*-Pent, 72%
42c R^1 = H, R^2 = *c*-Hex, 70%
42d R^1 = Me, R^2 = Ph, 91%
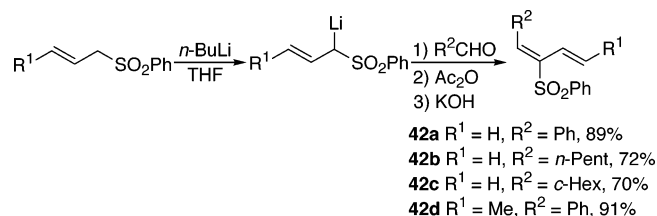
Treatment of **42b**−**c** with 1.5 equiv of (1-butene)ZrCp$_2$ at room temperature leads only to the *Z*-isomers **45** and **46** whatever the stereochemistry of the starting dienyl sulfones (i.e., **E-42d** and **Z-42d**, Scheme 11). Even the unstable *Z*-isomer **44** was preferentially formed from **42b** in this process with an excellent Z/E ratio of 95/5. The low yield obtained for **45** is attributed to the volatility of the resulting diene.

By analogy with the mechanistic pathway described for the enol ether **40** (Scheme 9), we believe that the transformation of **42a**−**c** also occurs via the formation of the β-metalated allenyl intermediate generated from the β-elimination of the corresponding zirconacyclopropane and subsequent rearrangement. However, the direct transformation of the vinyl sulfone moieties into dienyl zirconocenes without intervention of the terminal unsubstituted double bond cannot be ruled out at this stage,[25,26] particularly that when the more substituted dienyl sulfone **42e** (Scheme 11) was similarly treated with (1-butene)-ZrCp$_2$, a mixture of 3 isomers of undetermined geometry was obtained after hydrolysis.

To further increase the scope of the reaction, transmetalation of dienyl zirconium complexes such as **44Zr** into the corresponding dienyl organometallic derivatives was performed. To our surprise, when **44Zr** was transmetalated to copper derivatives by addition of CuCl·2LiCl for 1h at +45 °C, a complete isomerization of the dienyl system was found; that is, trans-**44Zr** is transmetalated into *cis*-**44Cu**, and then after hydrolysis, only the *E*-isomer of **44** is formed in 70% yield (Table 2). When heating the dienyl zirconocene **44Zr** at +50 °C, with or without added LiCl, no isomerization of the diene was detected.

As nothing is known on the exact nature of organocopper coming from organozirconocene derivatives, we must await further investigations to elucidate completely the mechanism of this transmetalation, but this isomerization was found to be general for all the examined cases (Table 2, **44**−**47Zr**). It should be noted that even when a secondary alkyl group is present on the dienyl system as in **46Zr** (Table 2, entry 3), the *E*-isomer is the major isomer after the transmetalation step in a ratio of 86/14 (which implies that before hydrolysis, the copper is cis

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Scheme 11. Preparation of Dienyl Zirconocenes from Conjugated Dienyl Sulfones
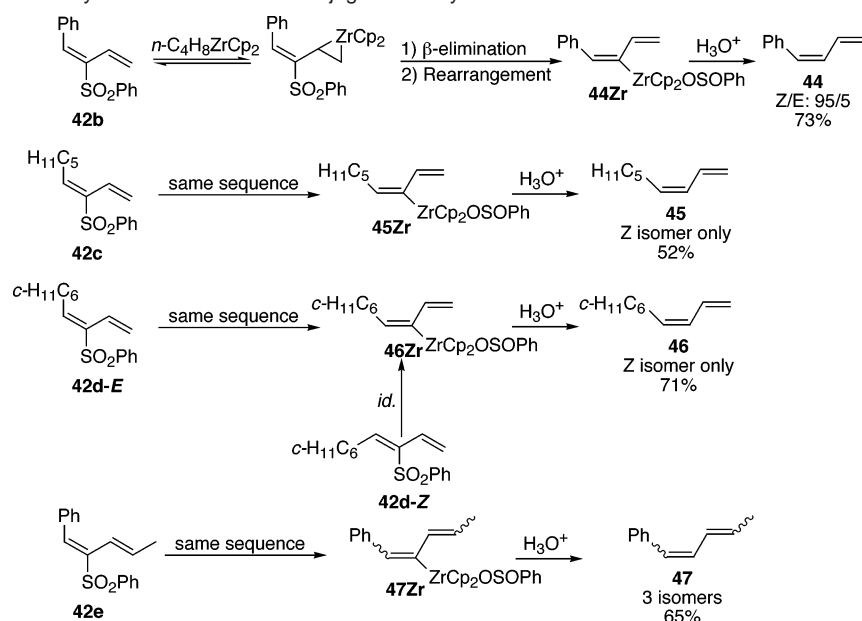
Table 2. Isomerization during the Transmetalation Reaction into Dienyl Copper Derivatives

| entry	compds	R^1	R^2	products	$E,E/Z,E$ ratio	yield^a(%)
1	*trans*-**44Zr**	Ph	H	**44**	>99/1	73
2	*trans*-**45Zr**	C_5H_{11}	H	**45**	80/20	48^b
3	*trans*-**46Zr**	c-C_6H_{11}	H	**46**	86/14	71
4	**47Zr**^{c}	Ph	CH_3	**47**	92/8	60

^{a} Yields of pure products after purification by chromatography on silica gel ^{b}low yield attributed to the volatility of **45** ^{c}**47Zr** is a mixture of three geometrical isomers.

to the secondary alkyl group). Moreover, from the three geometrical isomers of **47Zr** (Table 2, entry 4), this transmetalation-isomerization led mainly to the *E,E*- isomer **47** after hydrolysis (*E,E/Z,E*: 92/8).

The synthetic use of this isomerization was also investigated by reaction of the resulting dienyl copper derivatives with several different electrophiles as described in Scheme 12.

44Cu reacts via an S_N2' process with allyl chloride to give a unique *E*-isomer of the triene **48** and the geometrical mixture of **45** and **46Cu** gave, under the same experimental conditions, the two allylated products with the *E*-isomer as major product (it should be emphasized that although the transmetalation–isomerization occurs at +50 °C, the reactivity of the organo-copper remains intact in this process). The addition of methyl vinyl ketone or cyclohexenone in the presence of TMSCl[42] led to the 1,4 adducts **52** and **53** in 75 and 59% yield respectively as unique geometrical isomers. The palladium cross-coupling reaction of **44Cu** with alkynyl iodide and aryl iodide opens new routes to further functionalization between two sp^2 and sp^2–sp units as described for the preparation of **50** and **51**.

Scheme 12. Reactivity of the Dienyl Copper Derivatives
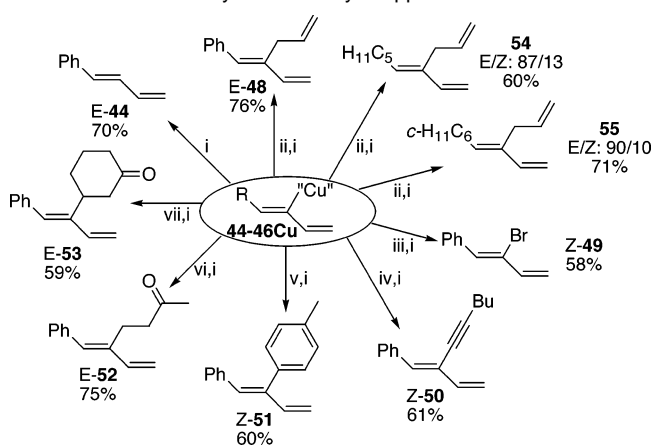
(i) H_3O^+, (ii) allyl chloride, (iii) NBS, (iv)1-iodo-1-hexyne, 5% Pd-(PPh$_3$)$_4$, (v) 4-iodotoluene, Pd(PPh$_3$)$_4$, (vi) methyl vinyl ketone, TMSCl, (vii) cyclohexenone, TMSCl.

In conclusion, we have reported a very easy and straightforward preparation of several metalated dienyl derivatives as unique geometrical isomers in only two chemical steps from commercially available or very accessible starting materials. This new methodology is based on a tandem allylic C–H bond activation-elimination sequence. Moreover, when the organo-metallic derivative is vinylic as well as allylic such as in **44**–**47Zr**, an unexpected reversal of the stereochemistry has been found during the zirconium to copper transmetalation step.

Supporting Information Available: Experimental procedures and spectra data of all compounds are available (93 pages, print/ PDF). This material is available free of charge via the Internet at http://pubs.acs.org

JA036751T

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