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Stereoselective Preparation of *E* Vinyl Zirconium Derivatives from *E* or *Z* Enol Ethers

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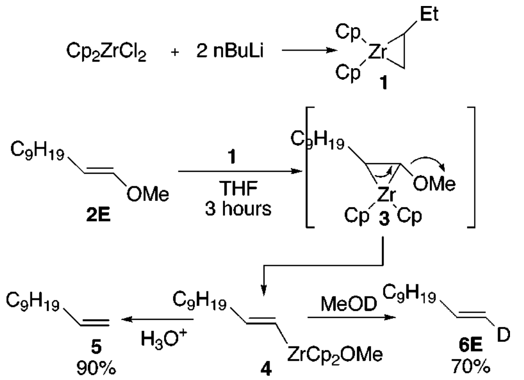
Since the discovery of a convenient method for the generation of low-valent zirconium species, synthetic organic transformations using "Cp_2Zr" have been extensively developed.[1] This reagent is easily prepared in situ by treatment of Cp_2ZrCl_2 with 2 equiv of *n*-butyllithium and is known as the Negishi reagent.[1] It has been shown to exist as a zirconocene−butene complex equivalent **1** (Scheme 1) and reacts with unsaturated compounds to form the corresponding zirconacycles.[2] It is also known that due to the oxophilic nature of zirconium metal, an easy elimination of alkoxy group in a β-position can be induced to form the unsaturated compound.[3] Accordingly, several allylic,[4] allenic,[5] γ-[6]and γ,γ-alkoxy allylic[7] zirconium species were prepared.[8] However, this concept of β-elimination was only sporadically used for the preparation of *vinyl* zirconium derivatives. The initial report was published by Takahashi et al. by reaction of 2-chloroalkene derivatives[9] with **1**, and more recently, this strategy has been successfully applied by Ichikawa and Minami[10] for the synthesis of fluorinated vinyl zirconium moieties. In both cases, a good leaving group was used (halide or tosyloxy groups) for the β-elimination and no information on the stereochemical outcome of this reaction was described.[11] As vinyl organometallic derivatives represent an important class of synthons for the creation of carbon−carbon bonds, strategies are well described and used.[12] However, the latter uses, most of the time, the corresponding halides as starting materials. So, a general method for the preparation of vinyl organometallic derivatives from unactivated enol ether is still needed.[13] We have recently described that the addition of zirconocene or titanocene derivatives to halogeno- or thiophenyl alkyne moieties gives, respectively, the functionalized alkynylmetal[14] or metallometallacyclopropene derivatives[15] (M = Ti or Zr), via an "addition−β-elimination" sequence. In this paper, we report the extension of this concept to the formation of vinyl organometallic derivatives (Scheme 1). We indeed found that this reaction occurs smoothly at room temperature in THF by the addition of the *E* methoxy enol ether **2**[16] to 1.5 equiv of zirconocene complex **1**. The vinyl zirconium derivative **4** is obtained quantitatively, as determined by gas chromatography analysis with internal standard. Hydrolysis of the reaction mixture give undec-1-ene **5** in 90% yield after purification as described in Scheme 1.

Scheme 1



The formation of a discrete organometallic species was checked by deuteriolysis of the reaction mixture and only the *E* isomer was obtained. The postulated mechanism for this reaction is that the in situ formed zirconocene derivative **1** reacts with the methoxy enol ether **2E**, via a ligand exchange, to give an unstable intermediate methoxyzirconacyclopropane derivative **3**.[17] Then, **3** undergoes a very fast β-elimination at room temperature to give the vinyl zirconium derivative **4**. An alternative mechanistic pathway could also be the oxidative addition of **1** into the vinylic carbon-methoxy bond. However, it can be ruled out since we do not observe any aromatic organometallic derivatives by treatment of anisole with **1**. Surprisingly, when the same reaction is performed on the *Z* enol ether (**2Z** instead of **2E**), the same *E* isomer **6** is obtained after treatment of the reaction mixture with MeOD (Scheme 2).[18]

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(11) The only available information was described in ref 9, footnote 20. A *J* value of 19 Hz was obtained (trans configuration) for a vinyl zirconium without a description of the stereochemistry of the starting material.

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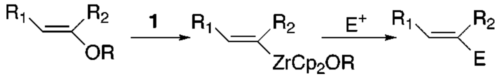
(17) All our attempts to isolate the hydrolyzed product of **3** failed.

(18) The reaction of vinyl zirconium derivatives with electrophiles occurs with retention of the stereochemistry.

10.1021/jo005561n CCC: $19.00

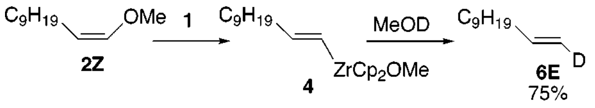
Table 1. Reaction of 1 with Enol Ethers and Trapping with Electrophiles



entries	R_1	R_2	OR	starting materials	*E*/*Z* ratio	electrophile	product	yield[a] (%)
1	C_9H_{19}	H	OMe	**2**	75/25	H_3O^+	**5**	90
2	C_9H_{19}	H	OMe	**2**	75/25	MeOD	**6**	70
3	C_9H_{19}	H	OMe	**2**	75/25	I_2	**7**	89
4	C_9H_{19}	H	OMe	**2**	75/25	PhI, CuCl 5% Pd(PPh$_3$)$_4$	**8**	75
5	C_9H_{19}	H	OtBu	**9**	80/20	MeOD	**6**	40
6	C_9H_{19}	H	OSitBuMe$_2$	**10**	65/35	I_2	**7**	75
7	Ph	H	OMe	**11**	70/30	H_3O^+	**12**	70
8	Ph	H	OMe	**11**	70/30	MeOD	**13**	75
9	Ph	H	OMe	**11**	70/30	I_2	**14**	70
10	Ph	H	OMe	**11**	70/30	allylCl 10% CuCl/2LiCl	**15**	60
11	H	Ph	OMe	**16**		MeOD	**17**	70

[a] Yield of isolated products after purification by column chromatography.

Scheme 2



So, whatever be the stereochemistry of the initial methoxy-enol ether, the reaction is >99% stereoselective but nonstereospecific, producing the *E* vinyl zirconium in good overall yields.

The scope of this reaction is relatively broad since methoxy enol ethers **2** and **11** derived respectively from aliphatic (entries 1 to 4, Table 1)[16] and aromatic aldehydes (entries 7−10, Table 1)[19] as well as methoxy enol ether **16** derived from ketone (entry 11, Table 1) undergo this formal "methoxyzirconium exchange". In all cases, only the *E* isomer was detected on the crude NMR. To check if the steric hindrance of the leaving group has an effect on the stereochemical outcome of this process, the reaction was also performed on the *ter*butoxy enol ether **9** (entry 5, Table 1).[20] Here again, only the *E* isomer was obtained after deuteriolysis albeit in lower yield [only 40% of **6** was obtained after 4 h at room temperature, the balance being the starting material (with the same *E*/*Z* ratio of 80/20)]. However, when the silyl enol ether **10** (entry 6, Table 1) was treated with **1**, the reaction occurred smoothly to give the corresponding vinyl zirconium derivative, which was trapped by iodine into **7** in 75% yield.[21] Moreover, alkenyl zirconocenes participate in a wide range of ligand transfer reactions after transmetalation.[22] These can be transmetalated into palladium species[23] and coupled with aromatic iodide (entry 4, Table 1)[24] or transmetalated into vinyl copper by addition of a catalytic amount of copper salt and reacted with classical electrophiles of copper chemistry as with allyl chloride (entry 10, Table 1).[25]

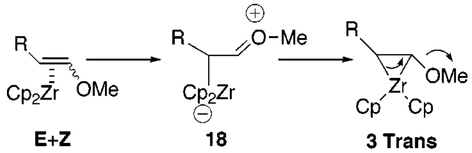


Figure 1.

These transmetalations reactions increase the scope of this reaction since several electrophiles, classical of the palladium or copper chemistry, can be introduced for the alkylation step. However, when tri-and tetrasubstituted enol ethers were treated with **1**, no reaction was observed.

Although the "addition−β-elimination" sequences described in Scheme 1 seem to be reasonable, more complicated intermediates are probably involved during the complexation between the methoxy enol ether and the zirconocene **1**. Our hypothesis is that the initial step proceeds most likely via a dipolar zirconate species represented by **18** (Figure 1),[26] and then isomerization should occur to give the trans methoxy zirconacyclopropane **3** before β-elimination. These types of nonconcerted paths for reactions of alkene with zirconocene complexes were already discussed in the literature by Negishi and Takahashi.[27] Moreover, no stereoisomerization of **2Z** was observed by using 10 mol % of ^{n}Bu$_2$ZrCp$_2$, which indicates that zirconocene **1** is not a catalyst for the isomerization of methoxy enol ether **2Z** into **2E** (and no other products were detected).

To probe further the interaction between the enol ethers and **1** via **18**, we thought that by reducing the potentiality to form the oxonium of the vinylic oxygen it would decrease the percentage of isomerization. For this purpose, we have prepared the vinylic carbamate **19**. We were pleased to find that the treatment of the geometrical mixture of the vinylic carbamate **19** (*E*/*Z* 57:43) with zirconocene **1**, gives, after iodinolysis the corresponding vinyl iodide **7** in a 60/40 *E*/*Z* ratio (Scheme 3). So, indeed only a slight isomerization was observed.[28]

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(19) Tzalis, D.; Koradin, C.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 6193.

(20) *tert*-Butoxy enol ether is easily prepared by carbocupration of the corresponding alkoxyallene derivative; see ref 16.

(21) Surprisingly, the behavior of the silane, (1,1-dimethylethyl) dimethyl[[1E/Z)-3-phenyl-1-propenyl]oxy] is totally different and a kinetic resolution occur; only the *E*-isomer reacts. These results will be reported in due course.

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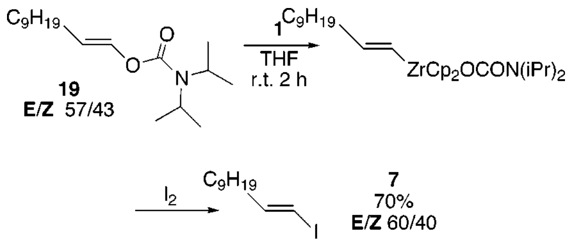
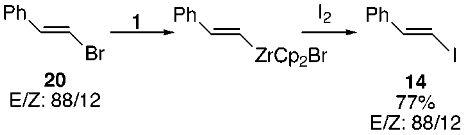
(26) An α-elimination and formation of carbene can also be operative. However, there is no special reason in this case to have only the *E* isomer of **4**.

(27) Negishi, E.-I.; Choueiry, D.; Nguyen, T. B.; Swanson, D. R.; Suzuki, N.; Takahashi, T. *J. Am. Chem. Soc.* **1994**, *116*, 9751.

Scheme 3



Scheme 4



Moreover, to confirm that the isomerization occurs effectively via a dipolar zirconate **18**, we have repeated the same experiment on the commercially available β-bromo styrene **20** with an *E*/*Z* ratio of 88/12. When the latter is treated first with the zirconocene equivalent **1** at room temperature for 3 h, and then with iodine, the expected β-iodo styrene **14** is obtained in 77% yield, as a mixture of two isomers in the same ratio that of the starting material (*E*/*Z* 88/12) (Scheme 4).[29] Clearly, when no oxonium is formed, we do not observe any isomerization.

In summary, we have demonstrated the first transformation of enol ethers into the corresponding vinyl zirconium derivatives. This reaction occurs stereoselectively, irrespective of the stereochemistry of the starting material. Moreover, due to the potential transmetalation step, a large variety of electrophiles can be added. However, when the vinylic carbamate or the β-bromo styrene are treated with the zirconocene complex **1**, the isomerization do not take place which can be attributed to a dipolar zirconate intermediate.

Further applications of the present reactions will be reported in due course.

Experimental Section

General Procedure. A solution of *n*-butyllitium in hexanes (1.6 M, 3.3 equiv) was added slowly to a solution of bis(cyclopentadienyl)zirconium dichloride (1.5 equiv) in dry THF at −78 °C. After the solution was stirred for 1 h at −78 °C, the enol ether was added (1 equiv) at −78 °C. The reaction mixture was allowed to warm to room temperature and stirred for 2.5−5 h. The quantitative formation of the adduct was checked by GC. Then, the solution was cooled to −20 °C, and the electrophile was added. The reaction was warmed to room temperature, and the mixture was diluted with ether and HCl 1 N. The aqueous phase was then extracted three times with ether. The combined organic phase was then washed successively with a solution of saturated aqueous sodium hydrogen carbonate, brine, and water (in case of addition of iodine, aqueous $Na_2S_2O_3$ was also used), dried over $MgSO_4$, and evaporated under reduced pressure. The residue obtained was finally purified by column chromatography on silica gel.

1-Undecene 5. Purification by chromatography on silica gel (eluent: hexane) gave a colorless liquid, yield 90%, spectrally identical with an authentic sample commercially available: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.87 (t, 3H, $J = 7$ Hz), 1.25 (m, 14 H), 2.04 (bq, 2H), 4.97 (m, 2H), 5.77 (m, 1H).

(*E*)-1-Deuterioundecene 6. Purification by chromatography on silica gel (eluent: hexane) gave a colorless liquid in 70% yield: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0,87 (t, 3H, $J = 7$ Hz), 1.25 (m, 14 H), 2.04 (d, 1H, $J = 15.2$ Hz), 4.97 (d, 1H, $J = 15.2$ Hz), 5.77 (m, 1H).

(*E*)-1-iodoundecene 7. Purification by chromatography on silica gel (eluent: hexane) gave a yellow liquid in 89% yield, spectrally identical with an authentic sample:[30] ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.86 (t, 3H, $J = 7$ Hz), 1.24 (m, 14H), 2.03 (bq, 2H, $J = 6.8$ Hz), 5.93 (d, 1H, $J = 14.2$ Hz), 6.48 (dt, 1H, $J = 6.8, 14.2$ Hz).

(*E*)-1-Phenyl-1-undecene 8. The general procedure was used as described above. When the formation of the vinyl zirconium was complete (checked by GC), 0.26 mL of phenyl iodide (481 mg, 2.36 mmol, 1 equiv), copper chloride (303 mg, 3.06 mmol, 1.3 equiv), and 5% of $Pd(PPh_3)_4$ (0.11 mmol, 136 mg) were added at room temperature. The solution was heated for 3 h at 50 °C. After usual treatment, the residue was purified by chromatography on silica gel (eluent: hexane) to give a colorless liquid in 75% yield, spectrally identical with an authentic sample:[31] ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.86 (t, 3H, $J = 7$ Hz), 1.26 (m, 14H), 2.03 (m, 2H), 5.48−5.62 (m, 1H), 5.91−6.02 (m, 1H), 7.05 (m, 5H).

Styrene 12. Purification by chromatography on silica gel (eluent: hexane) gave a colorless liquid, yield 70%, spectrally identical with a commercially available sample: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.29 (d, 1H, $J = 17.5$ Hz), 5.8 (d, 1H, $J = 17.5$ Hz), 6.74−6.81 (dd, 1H, $J = 10.8, 17.5$ Hz), 7.24−7.47 (m, 5H).

(*E*)-β-Deuteriostyrene 13. Purification by chromatography on silica gel (eluent: hexane) gave a colorless liquid, yield 75%, spectrally identical with an authentic sample:[32] ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 5.7 (d, 1H, $J = 17.5$ Hz), 6.7 (d, 1H, $J = 17.5$ Hz), 7.11−7.37 (m, 5H).

(*E*)-β-iodostyrene 14. Purification by chromatography on silica gel (eluent: hexane) gave a yellow liquid, yield 70%, spectrally identical with an authentic sample:[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.82 (d, 1H, $J = 15.5$ Hz), 7.2−7.33 (m, 5H), 7.42 (d, 1H, $J = 15.5$ Hz).

(*E*)-1-Phenyl-1,4-pentadiene 15. The general procedure was used as described above. When the formation of the vinyl zirconium was complete (checked by GC), 0.25 mL of allyl chloride (3.24 mmol, 1.5 equiv), copper chloride (0.22 mmol, 21 mg, 0.1 equiv), and lithium chloride (4.32 mmol, 183 mg, 2 equiv) were added at 0 °C. Then, the solution was stirred at 50 °C for 5 h. After usual treatment, the residue was purified by chromatography on silica gel (eluent: hexane) to give a colorless liquid, yield 60%, spectrally identical with an authentic sample:[34] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.01 (m, 2H), 5.11−5.22 (m, 2H), 5.93−6.03 (m, 1H), 6.26−6.33 (dt, 1H, $J = 6.3, 15.7$ Hz), 6.49 (d, 1H, $J = 15.7$ Hz), 7.25−7.49 (m, 5H).

α-Deuteriostyrene 17. Purification by chromatography on silica gel (eluent: hexane) gave a colorless liquid, yield 70%, spectrally identical with an authentic sample:[31] ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 5.22 (s, 1H), 5.8 (s, 1H), 7.24−7.47 (m, 5H).

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[28] The same reaction was also performed on acetoxy enol ether, but in this case, **1** reacts faster with the ester than with the double bond.

[29] As suggested by a reviewer, two different mechanisms might also operate for activation of enol ethers versus alkenyl halides. Although our mechanism is still speculative, the dipolar species such an **18** explain nicely our results.

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