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Preparation and Synthetic Transformation of Alkenyl Carbamates into Vinyl Zirconocene Derivatives

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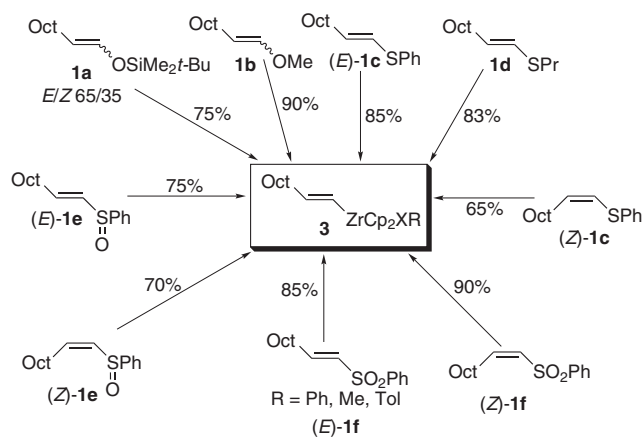
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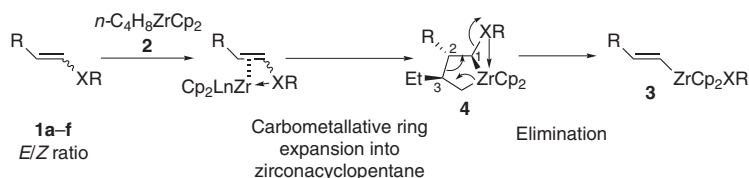
Abstract: The carbocupration reaction of alkenyl carbamates leads to the stereospecific preparation of polysubstituted alkenyl carbamates. Subsequent treatment of these enol carbamates with the Negishi reagent gave the corresponding vinyl zirconocene species.

Keywords: alkenyl carbamates, vinyl zirconocene derivatives, organocopper reagents

We have recently reported that heterosubstituted alkenes **1a–f** such as enol ether,¹ silyl enol ether,² vinyl-, alkyl-, and aryl sulfides, vinyl sulfoxides, and even vinyl sulfones³ were excellent candidates for the stereoselective preparation of alkenyl⁴ and conjugated dienyl⁵ organometallic derivatives.⁶ Typically, reactions were complete in a few hours at room temperature by treatment of the alkene with the Negishi reagent $C_4H_8ZrCp_2$ **2**⁷ (prepared in situ by reaction of the commercially available Cp_2ZrCl_2 with two equivalents of *n*-BuLi)⁸ with these alkenes (Scheme 1).



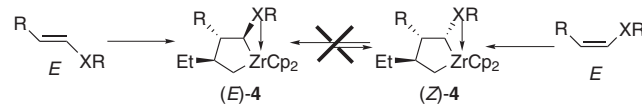
Scheme 1



Scheme 2

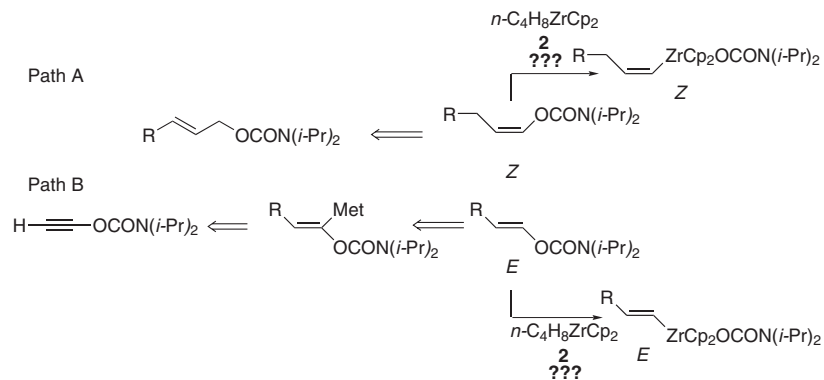
Interestingly, regardless of the stereochemistry of the starting heterosubstituted olefins **1a–f**, a complete isomerization reaction occurred to give the pure *trans*-vinyl zirconocene derivatives **3** stereospecifically. This isomerization has been rationalized as a carbometallative ring expansion between **1** and **2**, which leads to the corresponding five-membered ring zirconacycle **4** in which the carbon–heteroatom bond of the sp^3 -metallated center C_1 isomerizes to produce the most stable intermediate. Such isomerization could be due to an interaction between the heterosubstituent and the zirconium atom, which would produce a weakening of the C_1 –Zr bond facilitating the isomerization (Scheme 2).⁹ Thus, whatever the stereochemistry of **1**, the conformation of RX –Zr is always antiperiplanar to C_2 – C_3 before the elimination reaction.

Although this transformation leads to only one isomer, we were interested in developing a stereospecific transformation of heterosubstituted olefins into sp^2 -organometallic derivatives (*E*- and *Z*-olefins give *E*- and *Z*-vinyl metals, respectively). Following our hypothetical mechanism, we thought that stereospecificity could be achieved if we simply avoid the isomerization reaction of the zirconacycle intermediate (*Z*)-**4** into (*E*)-**4** as described in Scheme 3.



Scheme 3

Therefore, the challenging question was to find a configurationally stable geminal configuration between the sp^3 carbon–zirconium bond and the X –R bond at room temperature – the temperature at which our transformation proceeds. Fortunately, Hoppe had initially shown that the



Scheme 4

deprotonation of *O*-alkyl carbamate with *s*-BuLi leads to a configurationally stable organolithium derivative and later on, Beak extended the application of this method to *N*-Boc-pyrrolidines.¹⁰ Consequently, we decided to study the stereospecificity of a new unknown transformation, namely the conversion of *E*- and *Z*-vinyl carbamate into the corresponding *sp*²-organozirconocene derivatives (Scheme 4). The preparation of *Z*-vinyl (*N,N*-diisopropyl)carbamate was well known^{10a} (Scheme 4, path A) and its transformation into functionalized derivatives such as lactol,¹¹ acetylene,¹² aldehyde,¹³ *Z*-alkene,¹⁴ enyne,¹⁵ *Z*-silyl enol ether,¹⁶ and *Z*-vinyl triflate¹⁷ derivatives have found many applications. All of these methods were advantageously used in many total syntheses where the preparation of enantiomerically enriched *anti*-homoallylic alcohols was necessary,^{10a} but surprisingly, no transformation of the same *Z*-vinyl (*N,N*-diisopropyl)carbamate into organometallic was described.

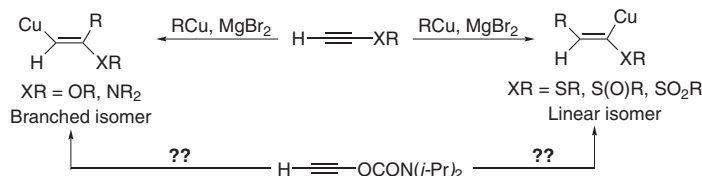
Moreover, the stereoselective preparation of pure *E*-vinyl (*N,N*-diisopropyl)carbamate has not been described in the literature.¹⁸ As stated earlier, we required an easy and straightforward access to either the *E*- or *Z*-isomer of vinyl (*N,N*-diisopropyl)carbamate, thus, we initially decided to develop a new stereoselective preparation of the *E*-isomer. Retrosynthetic analysis for the exclusive formation of the *E*-isomer shows that it should be easily prepared by a regioselective *syn* addition of substituents R and H across the alkyne. Obviously, the proton addition can be derived from the hydrolysis of a carbon–metal bond (Scheme 4, path B).

According to the retrosynthetic analysis described in Scheme 4, path B, a regio- and stereospecific carbometallation reaction of ethynyl carbamate should be the key reaction for the preparation of the *E*-enol carbamate. Among all the possible candidates for the carbometalla-

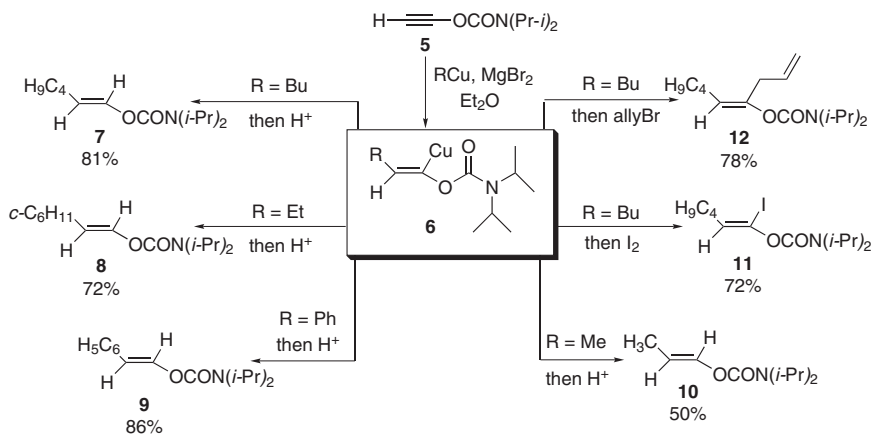
tion reaction,¹⁹ we were interested in using the carbocupration reaction since organocopper derivatives are known for their high regio-, stereo-, and chemoselectivity,²⁰ which enables them to add smoothly to the triple bond of various alkynes²¹ even in the presence of other functionalities.²² However, when organocopper derivatives are added to heterosubstituted alkynes, different possible regioisomers may be obtained; the directing effect of oxygen and nitrogen leads to the branched product (copper at the β -position relative to the heteroatom) whereas those of sulfur and phosphorus lead to the linear product (geminal relationship between copper and the heteroatom, Scheme 5).²³

Although alkynyl carbamate is an oxy-substituted alkyne and therefore should lead to the branched isomer, we thought that the electron-withdrawing effect of the carbamoyl group combined with its strong ability to coordinate organometallic derivatives should reverse the regiochemistry of the carbometallation reaction across the alkyne. Indeed, when ethynyl carbamate **5**, easily prepared from 2,2,2-tribromoethyl carbamate,²⁴ was treated with an organocopper reagent [RMgBr (1 equiv), CuBr (1 equiv), Et₂O, –30 °C, 30 min], the corresponding carbometallated product is obtained as described in Scheme 6.

The reaction is extremely fast since the carbometallated product **6** is formed after 90 minutes at –78 °C. Primary (R = Bu) as well as secondary alkyl groups (R = cyclohexyl) add cleanly to the alkyne furnishing only the pure *E*-isomers **7** and **8**, respectively, in good isolated yields. Even the phenyl and methyl groups, which are known to be very sluggish towards the carbocupration reaction,²⁰ lead to the expected addition product in good to moderate yields (**9** and **10**, respectively). The presence of a discrete organometallic was checked by the reaction of **6** (R = Bu) with either iodine or by reaction with allyl-



Scheme 5



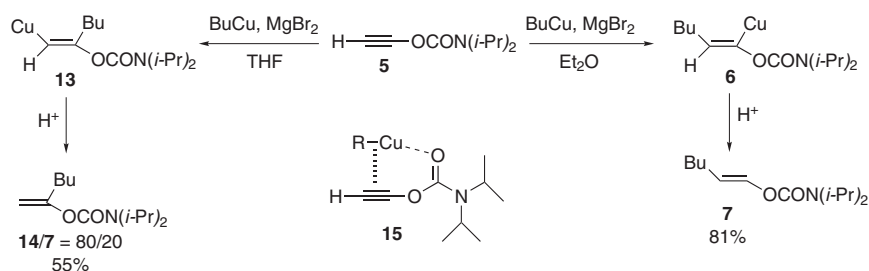
Scheme 6

bromide to give **11** and **12** in 72% and 78% yields, respectively.²⁵ Thus, a carbamoyl moiety attached to an ethynyl residue indeed reverses the regiochemistry of the carbocupration reaction (compare the regiochemistry for the alkoxy alkyne on Scheme 5 and ethynyl carbamate on Scheme 6) but the reaction has to be performed in a non-polar solvent such as diethyl ether. When more polar solvents such as THF are used, the classical regioisomer from the carbocupration of alkoxy-alkyne is obtained (the branched product is obtained in a 4:1 ratio as described in Scheme 7).

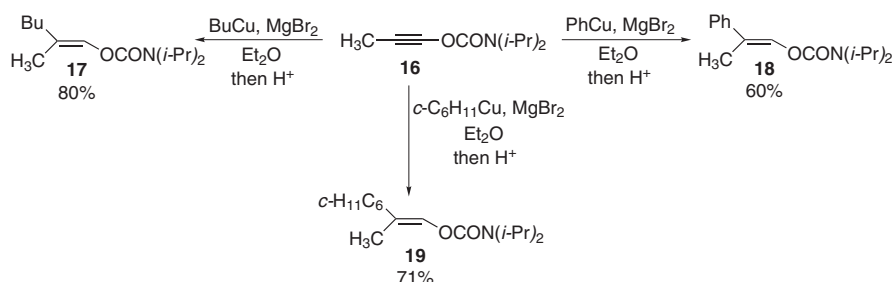
Internal delivery of the organometallic reagent via complex **15** is the suggested explanation for the anomalous regioselectivity observed for the carbocupration of **5**.²⁶ Thus, the branched isomer **13** resulted from the ‘normal’ regioselective addition, whereas the linear isomer **6** was the product of a directed reaction.²⁷ The carbamate–organocopper complex **15** is proposed to be the intermediate in the latter case.

Substituted alkynyl carbamate such as propynyl carbamate **16** also reacts easily with organocopper to afford stereospecifically the trisubstituted enol carbamates **17**–**19** as a single geometrical isomer (Scheme 8).²⁵

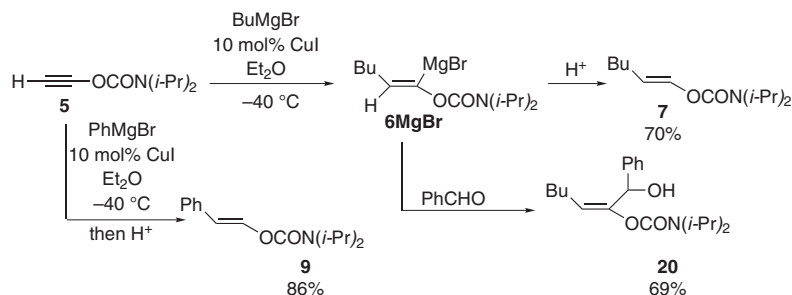
Finally, to extend the scope of this reaction, we were also interested in developing the copper-catalyzed carbomagnesiation reaction. Therefore, ethynyl carbamate **5** was reacted with a stoichiometric amount of alkylmagnesium halide in diethyl ether in the presence of copper iodide (10 mol%). The carbometallation reaction proceeds smoothly under these conditions (only the pure *E*-isomer was obtained) but at a slightly higher temperature ($-40\text{ }^\circ\text{C}$ instead of $-78\text{ }^\circ\text{C}$), which may be attributed to a slow transmetalation step between the chelated sp^2 organocopper to the corresponding organomagnesium derivative. Moreover, as described in Scheme 9, the reactivity of the newly formed sp^2 organometallic is completely different from the reactivity of the organocopper since **6MgBr** also reacts with aldehyde to give **20** in good isolated yield.



Scheme 7



Scheme 8



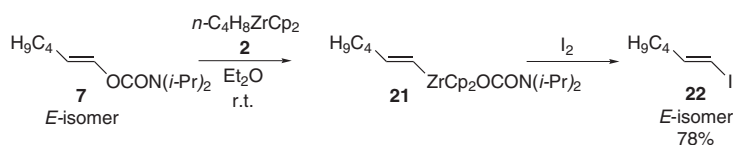
Scheme 9

With two simple methods in hand for the stereoselective preparation of the *E*-²⁵ and *Z*-isomers¹⁰ of diversely substituted enol carbamates, we came back to our initial pre-occupation, namely, the stereospecific transformation of vinyl carbamate into vinyl zirconocene derivatives. Originally, when the pure *E*-isomer **7** was treated with zirconocene reagent **2** in diethyl ether for 1.5 hours at 20 °C, the corresponding vinyl zirconocene **21** was easily obtained as determined by gas chromatography analysis of hydrolyzed aliquots. After addition of iodine, the corresponding *E*-vinyl iodide **22** was obtained in 78% isolated yield and as a single geometrical isomer (Scheme 10).

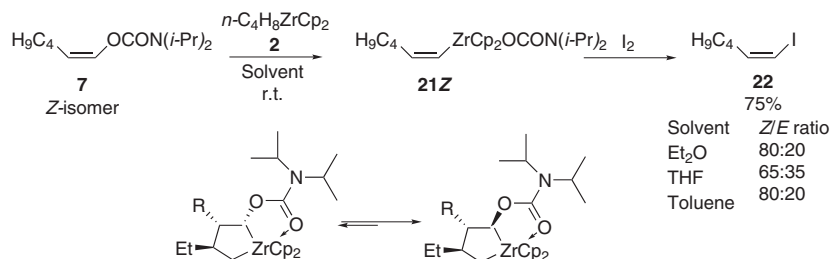
We, then, decided to study the behavior of the *Z*-vinyl carbamate **7** under the same experimental conditions. Therefore, when (*Z*)-**7** was subjected to our classical experimental conditions (1 h in Et₂O at r.t.) followed by iodinolysis, the corresponding *Z*-vinyl iodide **22** was obtained in 75% yield but with a *Z/E* ratio of 80:20 as described in Scheme 11.

A loss in stereospecificity is therefore observed. We initially checked that our starting material, namely the *Z*-vinyl carbamate **7**, does not undergo an isomerization reaction into the *E*-vinyl carbamate, before its transformation into vinyl zirconocene derivative **21**. Indeed, when the reaction described in Scheme 11 was trapped with iodine prior to completion, three products were observed; the *E*- and *Z*-isomers of the vinyl iodide **22** and the *Z*-vinyl carbamate **7**; no trace of the *E*-isomer of **7** was observed. From this we can conclude that the zirconocene complex

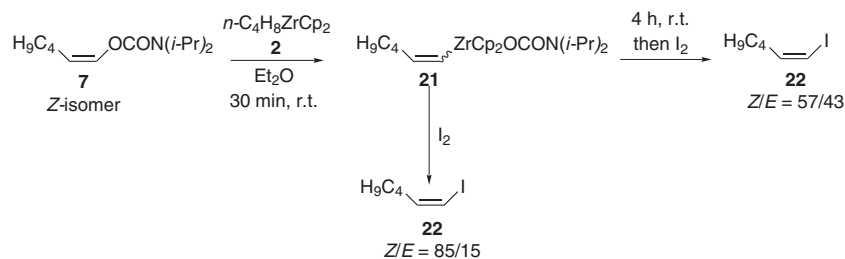
2 is not a catalyst for the isomerization of enol carbamate. Thus, following our working hypothesis, this isomerization may be also derived from a slow equilibration of the *Z*-zirconacyclopentane intermediate into its *E*-isomer (Scheme 11). When a more polar solvent such as THF is used in the reaction, the percentage of isomerization increased (*Z/E*, 65:35), which may be explained by the weaker intramolecular chelation of the zirconocene moiety by the carbamate in the zirconacyclopentane intermediate. On the other hand, when less polar solvents were used such as toluene, no improvement in the stereochemistry was detected. Diethyl ether was found to be the optimum solvent for the reaction. We were pleased to see that this transformation was very fast and complete in less than 30 minutes, the starting material completely disappeared resulting in the final product. Under these conditions, the *Z/E* ratio slightly increases to 85:15, which indicates that additional isomerization may occur as a result of a prolonged reaction time. To prove this hypothesis, the following experiment was carried out. The *Z*-vinyl carbamate **7** was treated with zirconocene reagent **2** in diethyl ether, after 30 minutes a complete transformation into the corresponding vinyl zirconocene **21** resulted. Then, half of the reaction was removed and treated with iodine. The crude NMR of this removed portion shows that the vinyl iodide has a *Z/E* ratio of 85:15. The remaining part of the reaction mixture was stirred for a further four hours at room temperature and finally quenched with iodine. In this portion, the *Z/E* ratio of the vinyl iodide **22**



Scheme 10



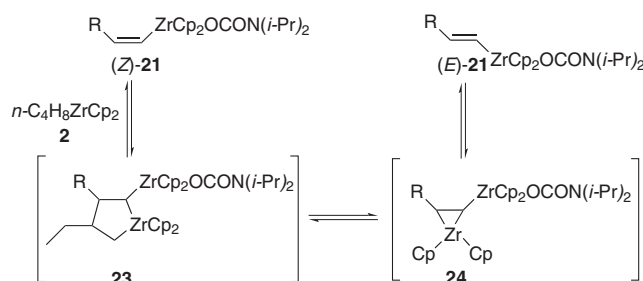
Scheme 11



Scheme 12

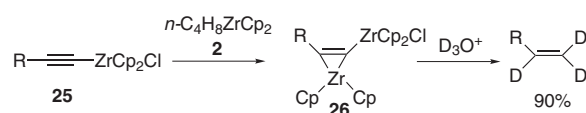
was found to be only 57:43, which shows that the *Z*-vinyl zirconocene **21** was indeed isomerized in situ (Scheme 12).

To rationalize the isomerization of the *Z*-vinyl zirconocene **21**, we assumed that a catalytic amount of free zirconocene reagent **2** reacts with **21** to give either the biszirconated species **23** or **24**, in which the carbon–zirconium bond has no reason to be configurationally stable and therefore undergoes partial isomerization (Scheme 13).



Scheme 13

The existence of a biszirconated species has already been shown when alkynyl zirconocene **25** was treated with an excess of **2** to give the corresponding tris-metallated alkene **26** as shown after deuteration (Scheme 14).²⁸



Scheme 14

In conclusion, we have initially described a new preparation for the stereospecific preparation of polysubstituted vinyl carbamate, as a single geometrical isomer, from alkynyl carbamates and organocopper reagents. We have been able to use these derivatives for the synthetically useful transformation of enol carbamate into *sp*²-organometallic derivatives by reaction with the Negishi reagent $\text{C}_4\text{H}_8\text{ZrCp}_2$. Under optimum experimental conditions, the *E*-isomer leads only to the *E*-vinyl zirconocene, whereas the *Z*-isomer gives a 85:15 mixture of *Z/E*-vinyl zirconocene. Further applications of these new methods will be reported in due course.

Experiments involving organometallics were carried out under a positive pressure of argon. All glassware was oven dried at 150 °C overnight and assembled quickly while hot under a stream of argon. Liquid N_2 was used as a cryogenic and all indicated temperatures are internal. Unless otherwise stated, a three-necked round-bottom flask equipped with an internal thermometer, a septum cap, and an argon inlet was used with a magnetic stirrer. Et_2O and THF were distilled from Na/benzophenone ketyl. Organolithium and organomagnesium reagents were titrated with *i*-BuOH (1 M, toluene) using 1,10-phenanthroline or 2,2'-biquinoyl as indicators, respectively. TLC was performed on silica gel coated plates, visualized either under a UV lamp or by using a 10% phosphomolybdic acid soln in EtOH followed by heating or sometimes with I_2 vapor.

NMR spectra have been recorded on either a Bruker AC 200, AC300, or AC 500 spectrometers in CDCl_3 as a solvent. Chemical shifts are reported in ppm relative to TMS as internal standard (0.1%) for ^1H NMR spectra and CDCl_3 for ^{13}C NMR spectra.

Stoichiometric Carbocupration; General Procedure (GP1)

To a soln of CuI (2.2 equiv) in anhyd solvent (10 mL) at -60 °C was added alkyl magnesium bromide (2.2 equiv). The reaction mixture was warmed to the indicated temperature and stirred for 30 min. Then, the reaction mixture was cooled to -78 °C and alkynyl carbamate **5** (1 equiv) in anhyd solvent was added dropwise. The reaction was warmed to the indicated temperature and stirred for an additional 90 min. After 90 min, the reaction was quenched by the addition of a sat. soln of NH_4Cl and a sat. soln of NH_4OH (30%) (1:2, 30 mL) and warmed to r.t. The phases were separated and the aqueous phase was extracted with Et_2O (3×50 mL). The combined organic layers were washed with a sat. soln of NH_4Cl and a sat. soln of NH_4OH (30%) (1:2, 50 mL) and dried over anhyd MgSO_4 .

Copper-Catalyzed Carbomagnesiation; General Procedure (GP2)

To a soln of CuI (0.1 equiv) in anhyd solvent (10 mL) at -60 °C was added alkyl magnesium bromide (2.2 equiv). The reaction mixture was warmed to -20 °C and stirred for 30 min. Then, the reaction mixture was cooled to -78 °C and alkynyl carbamate **5** (1 equiv) in anhyd solvent (10 mL) was added dropwise. The reaction soln was warmed to the indicated temperature and stirred for an additional 5 h. After 4 h, the reaction was quenched by the addition of a sat. soln of NH_4Cl and a sat. soln of NH_4OH (30%) (1:2, 30 mL) and warmed to r.t. The phases were separated and the aqueous phase was extracted with Et_2O (3×50 mL). The combined organic layers were washed with a sat. soln of NH_4Cl and a sat. soln of NH_4OH (30%) (1:2, 50 mL) and dried over anhyd MgSO_4 .

Diisopropylcarbamic Acid Hex-1-enyl Ester (7)

A soln of butylcopper (1.9 mmol) in Et_2O was prepared at -25 °C according to GP1. The carbocupration reaction of alkynyl carbamate **5** (0.145 g, 0.86 mmol) was performed at -65 °C. Purification by silica gel chromatography (EtOAc –hexane, 1:50) gave **7** in 81% yield (0.158 g).

^1H NMR (300 MHz, CDCl_3): δ = 6.96 (d, J = 17.25 Hz, 1 H), 5.25 (m, 1 H), 3.98 (m, 2 H), 1.96 (m, 2 H), 1.20 (m, 16 H), 0.85 (t, J = 7.02 Hz, 3 H).

^{13}C NMR (75 MHz, CDCl_3): δ = 152.1, 134.0, 111.0, 44.9 (2 C), 33.9, 26.0, 19.4 (4 C), 12.9.

Diisopropylcarbamic Acid 2-Cyclohexylvinyl Ester (8)

A soln of cyclohexylcopper (1.43 mmol) in Et_2O was prepared at -10°C according to GP1. The carbocupration reaction of alkynyl carbamate **5** (0.11 g, 0.65 mmol) was performed at -78°C . Purification by silica gel chromatography (EtOAc –hexane, 1:50) gave **8** in 72% yield (0.118 g).

^1H NMR (300 MHz, CDCl_3): δ = 6.99 (d, J = 12.55 Hz, 1 H), 5.18 (m, 1 H), 3.83 (m, 2 H), 1.3–1.04 (m, 23 H).

Diisopropylcarbamic Acid Styryl Ester (9)

A soln of phenylcopper (2.8 mmol) in Et_2O was prepared at -25°C according to GP1. The carbocupration reaction of alkynyl carbamate **5** (0.214 g, 1.27 mmol) was performed at -78°C . Purification by silica gel chromatography (EtOAc –hexane, 1:50) gave **9** in 86% yield (0.27 g).

^1H NMR (300 MHz, CDCl_3): δ = 7.84 (d, J = 12.83 Hz, 1 H), 7.31–7.16 (m, 5 H), 6.25 (d, J = 12.84 Hz, 1 H), 3.88 (m, 2 H), 1.24 (m, J = 6.7 Hz, 12 H).

^{13}C NMR (75 MHz, CDCl_3): δ = 151.7, 136.7, 134.0, 127.6 (2 C), 125.7, 124.9 (2 C), 111.5, 45.0 (2 C), 19.4 (4 C).

Diisopropylcarbamic Acid Propenyl Ester (10)

A soln of methylcopper (1.57 mmol) in Et_2O was prepared at -20°C according to GP1. The carbocupration reaction of alkynyl carbamate **5** (0.133 g, 0.786 mmol) was performed at -78°C . Purification by silica gel chromatography (EtOAc –hexane, 1:50) gave **10** as a liquid in 50% yield (0.722 g).

^1H NMR (500 MHz, CDCl_3): δ = 6.99 (d, J = 12.6 Hz, 1 H), 5.3 (m, 1 H), 4.04–3.77 (m, 2 H), 1.6 (d, J = 8.7 Hz, 3 H), 1.2 (d, 12 H, J = 10.5 Hz).

^{13}C (125.7 MHz, CDCl_3): δ = 155.0, 138.7, 108.6, 47.4 (2 C), 23.2 (4 C), 14.1.

Diisopropylcarbamic Acid 1-Iodohept-1-enyl Ester (11)

A soln of butylcopper (1.82 mmol) in Et_2O was prepared at -25°C according to GP1. The carbocupration reaction of alkynyl carbamate **5** (0.143 g, 0.85 mmol) was performed at -65°C . I_2 (3 equiv, 0.629 g, 2.48 mmol) in anhyd THF (5 mL) was added at -65°C , the reaction mixture was warmed to r.t., stirred for 15 min, and quenched as described in GP1. After classical work up, an additional washing of the organic layers was performed with a sat. aq soln of $\text{Na}_2\text{S}_2\text{O}_3$ (30 mL). Purification by silica gel chromatography (EtOAc –hexane, 1:100) gave **11** in 72% yield (0.216 g).

^1H NMR (300 MHz, CDCl_3): δ = 5.37 (t, J = 7.2 Hz, 1 H), 3.91–3.71 (m, 2 H), 2.00 (m, 2 H), 1.36 (m, 4 H), 1.154 (d, J = 6.6 Hz, 12 H), 0.82 (t, J = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, CDCl_3): δ = 152.4, 129.0, 102.3, 47.5–46.6 (2 C), 32.4, 30.9, 22.6, 22.0–20.8 (2 C), 14.5.

Diisopropylcarbamic Acid 1-Allylhex-1-enyl Ester (12)

A soln of butylcopper (1.9 mmol) in Et_2O was prepared at -25°C according to GP1. The carbocupration reaction of alkynyl carbamate **5** (0.150 g, 0.89 mmol) was performed at -65°C . Allyl bromide (3.3 equiv, 0.358 g, 2.96 mmol) was added at -65°C , the reaction mixture was warmed to -30°C , and stirred for 30 min. The reaction was quenched and work up carried out as described in GP1. Purification by silica gel chromatography (EtOAc –hexane, 1:100) gave **12** in 78% yield (185.6 g).

^1H NMR (300 MHz, CDCl_3): δ = 5.69 (m, 1 H), 5.07 (t, J = 7.5 Hz, 1 H), 4.95 (m, 2 H), 3.9–3.6 (m, 2 H), 2.96 (d, J = 6.6 Hz, 2 H), 1.96 (m, 2 H), 1.27–1.1 (m, 16 H), 0.79 (t, J = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, CDCl_3): δ = 153, 145.6, 133.5, 117.0, 115.9, 46.9 (2 C), 33.1, 31.5, 25.2, 21.6, 19.6 (4 C), 13.1.

Diisopropylcarbamic Acid 2-Methylhex-1-enyl Ester (17)

A soln of butylcopper (1.46 mmol) in Et_2O was prepared at -15°C according to GP1. The carbocupration reaction of alkynyl carbamate **16** (0.133 g, 0.73 mmol) was performed at -78°C . Purification by silica gel chromatography (EtOAc –hexane, 1:30) gave **17** in 80% yield (0.14 g).

^1H NMR (300 MHz, CDCl_3): δ = 6.85 (s, 1 H), 4.06–3.7 (m, 2 H), 1.9 (t, J = 7.5 Hz, 2 H), 1.6 (s, 3 H), 1.4–1.23 (m, 16 H), 0.87 (t, J = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, CDCl_3): δ = 153.6, 131.3 (2 C), 118.8, 39.0 (2 C), 33.9, 30.2, 22.6, 21.6–20.8 (4 C), 14.3, 14.2.

Diisopropylcarbamic Acid 2-Phenylpropenyl Ester (18)

A soln of phenylcopper (1.6 mmol) in Et_2O was prepared at -20°C according to GP1. The carbocupration reaction of alkynyl carbamate **16** (0.153 g, 0.84 mmol) was performed at -65°C . Purification by silica gel chromatography (EtOAc –hexane, 1:50) gave **18** in 60% yield (0.131 g).

^1H NMR (300 MHz, CDCl_3): δ = 7.50 (s, 1 H), 7.37–7.2 (m, 5 H), 4.08–3.8 (m, 2 H), 2.09 (s, 3 H), 1.27 (d, J = 11.1 Hz, 12 H).

^{13}C NMR (75 MHz, CDCl_3): δ = 152.9, 137.7, 130.9, 128.8 (2 C), 126.7, 125.9 (2 C), 118.3, 46.8, 45.9, 20.9 (4 C), 14.0.

Diisopropylcarbamic Acid 2-Cyclohexylpropenyl Ester (19)

A soln of cyclohexylcopper (1.2 mmol) in Et_2O was prepared at -10°C according to GP1. The carbocupration reaction of alkynyl carbamate **1b** (0.109 g, 0.6 mmol) was performed at -78°C . Purification by silica gel chromatography (EtOAc –hexane, 1:50) gave **19** as an oil in 71% yield (0.16 g).

^1H NMR (300 MHz, CDCl_3): δ = 6.84 (s, 1 H), 4.0–3.8 (m, 2 H), 1.95 (m, H), 1.65 (s, 3 H), 1.40–1.23 (m, 22 H).

^{13}C NMR (75 MHz, CDCl_3): δ = 152.8, 130.2, 123.0, 45.4 (2 C), 42.1, 33.0, 26.1, 25.5, 20.9 (4 C), 11.8.

Diisopropylcarbamic Acid 1-Butylvinyl Ester (14)

A soln of butylcopper (2.07 mmol) in THF was prepared at -20°C according to GP1. The carbocupration reaction of alkynyl carbamate **5** (0.176 g, 1.03 mmol) was performed at -78°C . Purification by silica gel chromatography (EtOAc –hexane, 1:50) gave **14** as an oil in 55% yield (0.234 g).

^1H NMR (500 MHz, CDCl_3): δ = 4.68 (s, 1 H), 4.64 (s, 1 H), 4.08–3.78 (m, 2 H), 2.28 (t, J = 8 Hz, 2 H), 1.47–1.34 (m, 4 H), 1.23 (d, J = 11 Hz, 12 H), 0.92 (t, J = 7 Hz, 3 H).

^{13}C NMR (125.7 MHz, CDCl_3): δ = 158.7, 118.9, 101.6, 48.1 (2 C), 35.2, 30.5, 24.0, 22.5 (4 C), 15.8.

Diisopropylcarbamic Acid Hex-1-enyl Ester (7)

A soln of BuMgBr and CuI in Et_2O was prepared at -20°C according to GP2. The Cu-catalyzed carbomagnesiation reaction of alkynyl carbamate **5** (0.148 g, 0.88 mmol) was performed at -40°C . Purification by silica gel chromatography (EtOAc –hexane, 1:50) gave **7** in 70% yield (0.14 g). See physical data reported for the stoichiometric procedure.

Diisopropylcarbamic Acid 1-(Hydroxyphenylmethyl)hex-1-enyl Ester (20)

A soln of BuMgBr and CuI in Et_2O was prepared at -20°C according to GP2. The carbocupration reaction of alkynyl carbamate **5**

(0.159 g, 0.94 mmol) was performed at -40°C . Benzaldehyde (2 equiv, 0.200 g, 1.89 mmol) was added at -70°C , the reaction mixture was warmed to -60°C , and stirred for 1 h. The reaction was quenched and work up carried out as described in GP2. Purification by silica gel chromatography (EtOAc–hexane, 1:10) gave **20** in 69% yield (0.216 g).

$^1\text{H NMR}$ (300 MHz, CDCl_3): δ = 7.45 (d, J = 8.7 Hz, 1 H), 7.09–6.9 (m, 5 H), 5.78 (d, J = 6.9 Hz, 1 H), 5.68 (d, J = 7.8 Hz, 1 H), 5.23 (t, J = 7.8 Hz, 1 H), 3.47 (m, 1 H), 3.22 (m, 1 H), 2.02 (m, 2 H), 1.12 (m, 4 H), 0.88 (m, 12 H), 0.68 (t, J = 6.9 Hz, 3 H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ = 155.3, 148.3, 140.8, 127.5 (2 C), 126.4, 125.4 (2 C), 122.0, 69.0, 46.1, 45.7, 31.4, 25.7, 21.9, 20.3–19.6 (4 C), 13.5.

Diisopropylcarbamic Acid Styryl Ester (9)

A soln of PhMgBr and CuI in Et_2O was prepared at -20°C according to GP2. The Cu-catalyzed carbomagnesiation reaction of alkenyl carbamate **5** (0.148 g, 0.88 mmol) was performed at -40°C . Purification by silica gel chromatography (EtOAc–hexane, 1:50) gave **9** in 86% yield (0.175 g). See physical data reported for the stoichiometric procedure.

Transformation of Vinylic Carbamate into sp^2 -Organozirconocene Derivatives; General Procedure

A soln of $n\text{-BuLi}$ (3 equiv) in hexane was added slowly to a soln of ZrCp_2Cl_2 (1.5 equiv) in anhyd solvent (10 mL) at -78°C . Then, the reaction mixture was warmed to 0°C , stirred for 5 min, and cooled again to -78°C . To this soln, vinyl carbamate (1 equiv) was added dropwise in anhyd solvent (3 mL). The reaction mixture was allowed to warm to r.t. and stirred for the indicated time. The formation of the adduct was checked by gas chromatography. Then, the reaction mixture was cooled to 0°C and solid I_2 (2 equiv) was added. The mixture was warmed to r.t., stirred for 1 h, then cooled to 0°C , and quenched with a 1 M aq soln of HCl (30 mL). The reaction was warmed to r.t. and the phases were separated. The aqueous phase was extracted with Et_2O (3×50 mL) and the combined organic layers were washed with a sat. soln of $\text{Na}_2\text{S}_2\text{O}_3$ (50 mL), and dried over anhydrous MgSO_4 . The solvents were evaporated under reduced pressure. All the physical data correlate with those of authentic samples.^{29,30}

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References

- (1) Liard, A.; Marek, I. *J. Org. Chem.* **2000**, *65*, 7218.
- (2) Liard, A.; Kaftanov, J.; Chechik, H.; Farhat, S.; Morlender-Vais, N.; Averbuj, C.; Marek, I. *J. Organomet. Chem.* **2001**, *624*, 26.
- (3) Farhat, S.; Marek, I. *Angew. Chem. Int. Ed.* **2001**, *40*, 1410.
- (4) (a) Farhat, S.; Zouev, I.; Marek, I. *Tetrahedron* **2004**, *60*, 1329. (b) Chinkov, N.; Chechik, H.; Majumdar, S.; Liard, A.; Marek, I. *Synthesis* **2002**, 2473.
- (5) (a) Chinkov, N.; Majumdar, S.; Marek, I. *J. Am. Chem. Soc.* **2002**, *124*, 10282. (b) Canchehui, B.; Bertus, P.; Szymoniak, J. *Synlett* **2001**, 123. (c) Nicka, N.; Majumdar, S.; Marek, I. *J. Am. Chem. Soc.* **2003**, *125*, 13258.
- (6) Chinkov, N.; Marek, I. In *Stereoselective Synthesis of Dienyl Zirconocene Complexes*, In *Topics in Organometallic Chemistry*, 10; Marek, I., Ed.; Springer-Verlag: Berlin/Heidelberg, **2004**, 133.
- (7) For reviews, see (a) Negishi, E.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1988**, *71*, 755. (b) Negishi, E.; Takahashi, T. *Acc. Chem. Res.* **1994**, *27*, 124. (c) Negishi, E.; Kondakov, D. Y. *Chem. Soc. Rev.* **1996**, *26*, 417.
- (8) *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, **2002**.
- (9) Ward, A. S.; Mintz, E. A.; Kramer, M. P. *Organometallics* **1988**, *7*, 8.
- (10) (a) Hense, T.; Hoppe, D. *Angew. Chem. Int. Ed.* **1997**, *36*, 2282. (b) Kerrick, S. T.; Beak, P. *J. Am. Chem. Soc.* **1991**, *113*, 9708.
- (11) (a) Hoppe, D.; Hanko, R.; Bronneke, A.; Lichtenberg, F.; van Hulslen, E. *Chem. Ber.* **1985**, *118*, 2822. (b) Berque, I.; Le Menez, P.; Razon, P.; Anies, C.; Pancrazi, A.; Ardisson, J.; Neuman, A.; Prange, T.; Brion, J. D. *Synlett* **1988**, 1135.
- (12) (a) Pimm, A.; Kocienski, P.; Street, S. D. A. *Synlett* **1992**, 886. (b) Ferezou, J. P.; Julia, M.; Li, Y.; Liu, L. W.; Pancrazi, A. *Bull. Soc. Chim. Fr.* **1995**, *132*, 428. (c) Smith, N. D.; Kocienski, P. J.; Street, S. D. A. *Synthesis* **1996**, 652.
- (13) (a) Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 932. (b) Hoppe, D.; Zschage, O. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 69. (c) Zschage, O.; Hoppe, D. *Tetrahedron* **1992**, *48*, 8389. (d) Hoppe, D.; Hense, T. *Angew. Chem. Int. Ed.* **1997**, *36*, 2282. (e) Paulsen, H.; Hoppe, D. *Tetrahedron* **1992**, *48*, 5667. (f) Berque, I.; Le Menez, P.; Razon, P.; Mahuteau, J.; Ferezou, J. P.; Pancrazi, A.; Ardisson, J.; Brion, J. D. *J. Org. Chem.* **1999**, *64*, 373.
- (14) (a) Kocienski, P.; Dixon, N. J. *Synlett* **1989**, 52. (b) Wadman, S.; Whitby, R.; Yeates, C.; Kocienski, P.; Cooper, K. *J. Chem. Soc., Chem. Commun.* **1987**, 241. (c) Poree, F. H.; Clavel, A.; Betzer, J. F.; Pancrazi, A.; Ardisson, J. *Tetrahedron Lett.* **2003**, *44*, 7553.
- (15) Madec, D.; Pujol, S.; Henryon, V.; Ferezou, J. P. *Synlett* **1995**, 435.
- (16) Madec, D.; Henryon, V.; Ferezou, J. P. *Tetrahedron Lett.* **1999**, *40*, 8103.
- (17) Poree, F. H.; Barbion, J.; Dhulut, S.; Betzer, J. F.; Pancrazi, A.; Ardisson, J. *Synthesis* **2004**, 3017.
- (18) For mixture of isomers, see: (a) Olofson, R. A.; Wooden, G. P.; Marks, J. T. Eur. Pat. 104984, **1984**; *Chem. Abstr.* **1984**, *101*, 190657u. (b) Franco-Filipasic, B. R.; Patarcity, R. *Chem. Ind.* **1969**, *8*, 166. (c) Shimizu, M.; Tanaka, E.; Yoshioka, H. *J. Chem. Soc., Chem. Commun.* **1987**, 136. (d) Olofson, R. A.; Schnur, R. C.; Bunes, L.; Pepe, J. P. *Tetrahedron Lett.* **1977**, 1567. (e) Lee, L. H. *J. Org. Chem.* **1965**, *30*, 3943. (f) Olofson, R. A.; Bauman, B. A.; Vancowicz, D. J. *J. Org. Chem.* **1978**, *43*, 752. (g) Mahe, R.; Dixneuf, P. H.; Lecolier, S. *Tetrahedron Lett.* **1986**, *27*, 6333. (h) Mahe, R.; Sasaki, Y.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1989**, *54*, 1518. (i) Hofer, J.; Doucet, H.; Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* **1999**, *32*, 311. (j) Rohr, M.; Geyer, C.; Wandeler, R.; Schneider, M. S.; Murphy, E. F.; Baiker, A. *Green Chem.* **2001**, *3*, 123. (k) Sengupta, S.; Snieckus, V. *J. Org. Chem.* **1990**, *55*, 5680. (l) Superchi, S.; Sotomayor, N.; Miao, G.; Joseph, B.; Snieckus, V. *Tetrahedron Lett.* **1996**, *37*, 6057. (m) Superchi, S.; Sotomayor, N.; Miao, G.; Joseph, B.; Campbell, M. G.; Snieckus, V. *Tetrahedron Lett.* **1996**, *37*, 6061.
- (19) For recent reviews on carbometallation reactions, see: (a) Marek, I.; Chinkov, N.; Banon-Tenne, D. In *Carbometallation Reactions*, In *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, **2004**, 395. (b) Banon-Tenne, D.; Marek, I. In *Carbometallation Reactions of Zinc Enolate Derivatives*, In *Transition Metals for Organic Synthesis*;

- Beller, M.; Bolm, C., Eds.; Wiley-VCH: Weinheim, **2004**, 563. (c) Marek, I. *J. Chem. Soc., Perkin. Trans. 1* **1999**, 535.
- (20) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841.
- (21) For theoretical calculations, see: (a) Nakamura, E.; Mori, S.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4887. (b) Mori, S.; Nakamura, E. *J. Mol. Struct.* **1999**, *5*, 1534.
- (22) Achyutha Rao, S.; Knochel, P. *J. Am. Chem. Soc.* **1992**, *114*, 7579.
- (23) (a) Normant, J. F.; Alexakis, A.; Commercon, A.; Cahiez, G.; Villieras, J. *C. R. Seances Acad. Sci., Ser. C* **1974**, 279, 763. (b) Vermeer, P.; Meijer, J.; de Graaf, C. *Recl. Trav. Chim. Pays-Bas* **1974**, *93*, 24. (c) Meijer, J.; Westmijze, H.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 102. (d) Alexakis, A.; Cahiez, G.; Normant, J.; Villieras, J. *Bull. Soc. Chim. Fr.* **1977**, 693.
- (24) (a) Gralla, G.; Wibbeling, B.; Hoppe, D. *Org. Lett.* **2002**, *4*, 2193. (b) Gralla, G.; Wibbeling, B.; Hoppe, D. *Tetrahedron Lett.* **2003**, *44*, 8979. (c) Hoppe, D.; Gonschorrek, C. *Tetrahedron Lett.* **1987**, *28*, 785. (d) Egert, E.; Beck, H.; Schmidt, D.; Gonschorrek, C.; Hoppe, D. *Tetrahedron Lett.* **1987**, *28*, 789.
- (25) Chechik-Lankin, H.; Marek, I. *Org. Lett.* **2003**, *5*, 5087.
- (26) For some similar examples, see: (a) Alexakis, A.; Normant, J. F.; Villieras, J. *J. Organomet. Chem.* **1975**, *96*, 471. (b) Alexakis, A.; Normant, J. F.; Villieras, J. *J. Mol. Catal.* **1975**, *1*, 43. (c) Alexakis, A.; Commercon, A.; Coulentianos, C.; Normant, J. F. *Tetrahedron* **1984**, *40*, 715.
- (27) Hoveyda, A.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.
- (28) (a) Marek, I. *Chem. Rev.* **2000**, *100*, 2887. (b) Averbuj, C.; Kaftanov, J.; Marek, I. *Synlett* **1999**, 1939. (c) Kaftanov, J.; Averbuj, C.; Vais-Morlender, N.; Liard, A.; Marek, I. *Polyhedron* **2000**, *19*, 563.
- (29) On, H. P.; Lewis, W.; Zweifel, G. *Synthesis* **1981**, 999; 1-hexene-1*E*-iodo, registry number: 16644-98-7.
- (30) (a) Brown, H. C.; Somayaji, V.; Richard, B. *Synthesis* **1984**, 919. (b) Alexakis, A.; Cahiez, G.; Normant, J. F. *Org. Synth.* **1990**, *Vol. VII*, 290, 1-hexene-1*E*-iodo, registry number: 16644-98-7.