

Communication

Carbozincation of Substituted 2-Alkynylamines, 1-Alkynylphosphines, 1-Alkynylphosphine Sulfides with Et₂Zn in the Presence of Catalytic System of Ti(O-*i*Pr)₄ and EtMgBr

Rita N. Kadikova *, Ilfir R. Ramazanov, Azat M. Gabdullin, Oleg S. Mozgovoï and Usein M. Dzhemilev

Institute of Petrochemistry and Catalysis of Russian Academy of Sciences, 141 Prospekt Oktyabrya, 450075 Ufa, Russia; ilfir.ramazanov@gmail.com (I.R.R.); saogabdullinsao@gmail.com (A.M.G.); skill15@mail.ru (O.S.M.); ink@anrb.ru (U.M.D.)

* Correspondence: kadikritan@gmail.com; Tel.: +7-(347)-284-27-50

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Abstract: The EtMgBr and Ti(O-*i*Pr)₄-catalyzed ethylzincation of 1-alkynylphosphine sulfides with Et₂Zn in diethyl ether followed by hydrolysis and deuteroysis affords corresponding β,β-disubstituted 1-alkenylphosphine sulfides with high yield. The EtMgBr and Ti(O-*i*Pr)₄-catalyzed reaction of 2-alkynylamines, 1-alkynylphosphines, and 1-alkenylphosphine sulfides with Et₂Zn in various solvents was studied. It has been found that the reaction of 2-alkynylamines and 1-alkynylphosphines in methylene chloride, hexane, toluene, benzene, and anisole leads to the selective formation of 2-alkenylamines and 1-alkenylphosphine oxides after oxidation with H₂O₂.

Keywords: ethylzincation; 1-alkynylphosphine sulfides; 1-alkynylphosphines; 2-alkynylamines; 2-zincoethylzincation; titanium catalysis; diethylzinc

1. Introduction

Recently we found that the reaction of 1-alkynylphosphines and substituted propargylamines with Et₂Zn in the presence of catalytic amounts of reagents, such as titanium(IV) isopropoxide and ethylmagnesium bromide, gives products of triple bond 2-zincoethylzincation [1]. Our study supplements Negishi's work on Ti-Mg-catalyzed cyclozincation of α,ω-enynes with Et₂Zn well [2]. It is known that Cu-, Ni-, Co-, and Ru-catalyzed carbozincation of alkynyl sulfoximines, alkynyl sulfones [3], 1-alkynyl sulfoxides [4], propargylic ethers [5], propargyl alcohols [6], and ynamides [7,8] is an effective tool for the synthesis of polysubstituted functionalized olefins. As regards the carbozincation of inactivated alkynes, a limited number of examples are reported in the literature. Ni-catalyzed stereoselective carbozincation of but-1-yn-1-ylbenzene with Ph₂Zn is known [9], as well as Co-catalyzed allylzincation of aryl alkynes [10]. As to the effective carbozincation of dialkyl substituted alkynes, only ethylzincation [6] and allylzincation [11] of dec-5-yne in the presence of stoichiometric amounts of Cp₂ZrI₂ were described in the literature. It should be emphasized that the use of a catalytic system consisting of EtMgBr and Ti(O-*i*Pr)₄ for 2-zincoethylzincation of α,ω-enynes was first reported by Negishi [2]. Before our study, no examples of carbozincation of alkynylphosphines were known. As regards carbozincation of *N*-containing alkynes, only one example of diastereoselective carbozincation of lithiated (*R*)-(1)-*N*-methyl-*N*-propargyl-1-phenylethylamine with crotylzinc bromide was reported [12]. Therefore, further investigation of the scope of applicability of Ti-Mg-catalyzed carbozincation of functionally substituted acetylene derivatives was of considerable interest. In view of the high demand for ligands based on phosphines as well as their derivatives in

organometallic and coordination chemistry [13,14], we studied, first of all, the catalytic carbozincation of 1-alkynylphosphine oxides and -phosphine sulfides.

2. Results and Discussions

2.1. Ti-Mg-Catalyzed Carbozincation of Substituted 1-Alkynylphosphine Sulfides with Et_2Zn

Unfortunately, none of our attempts to perform carbozincation of substituted 1-alkynylphosphine oxides [diphenyl(phenylethynyl)phosphine oxide, hept-1-yn-1-yl(diphenyl)phosphine oxide] with 2.5 equivalents of Et_2Zn (1 M in hexane) in the presence of 0.15 equivalent of $\text{Ti}(\text{O-}i\text{Pr})_4$ (0.3 M in hexane) and 0.2 equivalent of EtMgBr (2.5 M in Et_2O) in diethyl ether solution at room temperature met with success. However, 1-alkynylphosphine sulfides (hex-1-yn-1-yl(diphenyl)phosphine sulfide, hept-1-yn-1-yl(diphenyl)phosphine sulfide, oct-1-yn-1-yl(diphenyl)phosphine sulfide) proved to be reactive in this reaction. We found that 1-alkynylphosphine sulfides **1** react with 2.5 equivalents of Et_2Zn (1 M in hexane) in the presence of 0.2 equivalent of EtMgBr (2.5 M in Et_2O) and 0.15 equivalent of $\text{Ti}(\text{O-}i\text{Pr})_4$ (0.3 M in hexane) in diethyl ether at room temperature for 18 h to give, after hydrolysis or deuterolysis, the corresponding substituted Z-1-alkenylphosphine sulfides **3a–c** and **4a** in high yields (Figure 1).

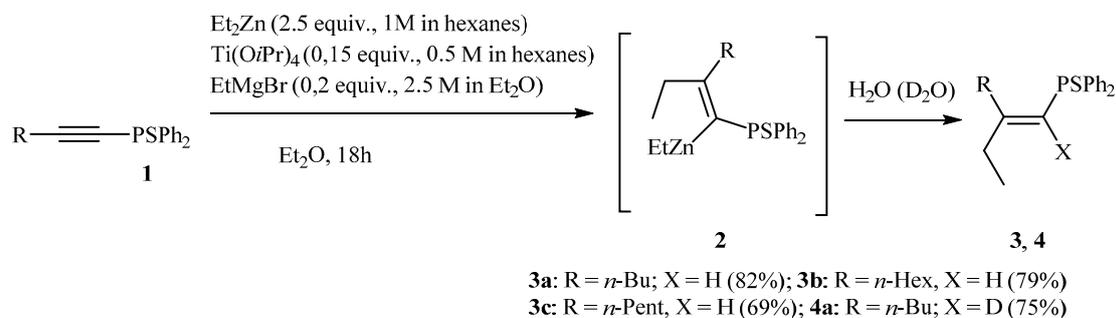


Figure 1. Ti-Mg-catalyzed carbozincation of substituted 1-alkynylphosphine sulfides with Et_2Zn in Et_2O .

The crucial difference from the reaction of 1-alkynylphosphines reported in our previous study [1] is that 1-alkynylphosphine sulfides are converted to ethylzincation rather than 2-zincoethylzincation products under the same conditions. In our opinion, the formation of ethylzincation products from alkyne phosphine sulfides proceeds in the following way. According to the presented Figure 2, fast ligand exchange between titanium(IV) isopropoxide and ethylmagnesium bromide yields an unstable diethyltitanium compound, which is then converted to a titanacyclopropane intermediate (titanium(II)–ethylene complex). Generation of a titanacyclopropane complex upon the reaction of Grignard reagents with titanium (IV) alkoxides was first suggested by Kulinkovich [15]. According to Figure 2, the subsequent insertion of 1-alkynylphosphine sulfide into the titanium-carbon bond of titanacyclopropane intermediate **A** results in the formation of titanacyclopentene intermediate **B**. The ligand exchange between intermediate **B** and the Et_2Zn molecule yields bimetallic intermediate **C**. The formation of a similar bimetallic complex is postulated in the Zr-catalyzed ethylmagnesiumation of inactivated alkenes [16]. The subsequent hydrogen transfer from the ethyl group at the titanium atom of the bimetallic complex **C** regenerates the titanacyclopropane intermediate and affords ethylzincation product **D**.

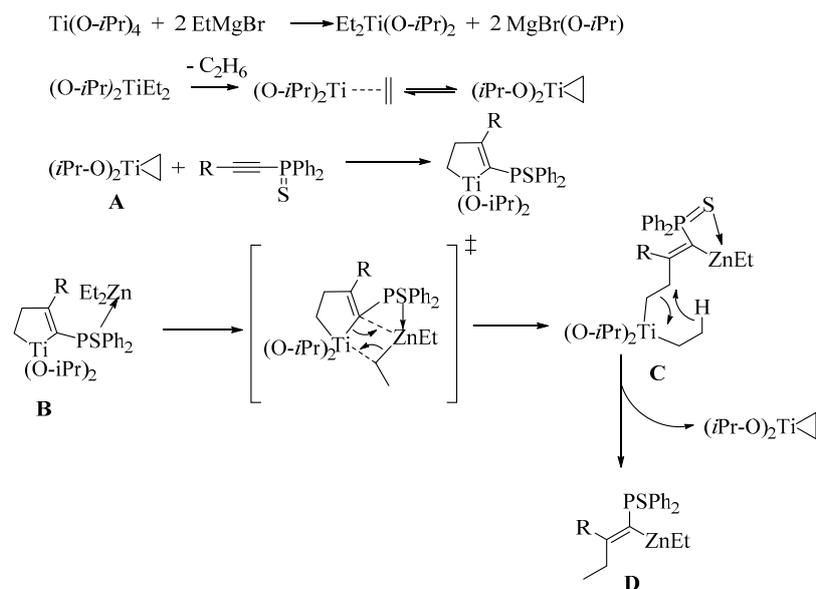


Figure 2. The plausible mechanism of Ti-Mg-catalyzed carbozincation of substituted 1-alkynylphosphine sulfides with Et_2Zn .

Unlike reactions of alkyl-substituted alkynylphosphine sulfides, the reaction of (cyclopropylethynyl) diphenylphosphine sulfide is not regioselective and gives a mixture of regioisomers of 1-alkenylphosphines **5** and **6** with *Z*-configuration of the double bond in 1:1 ratio (Figure 3).

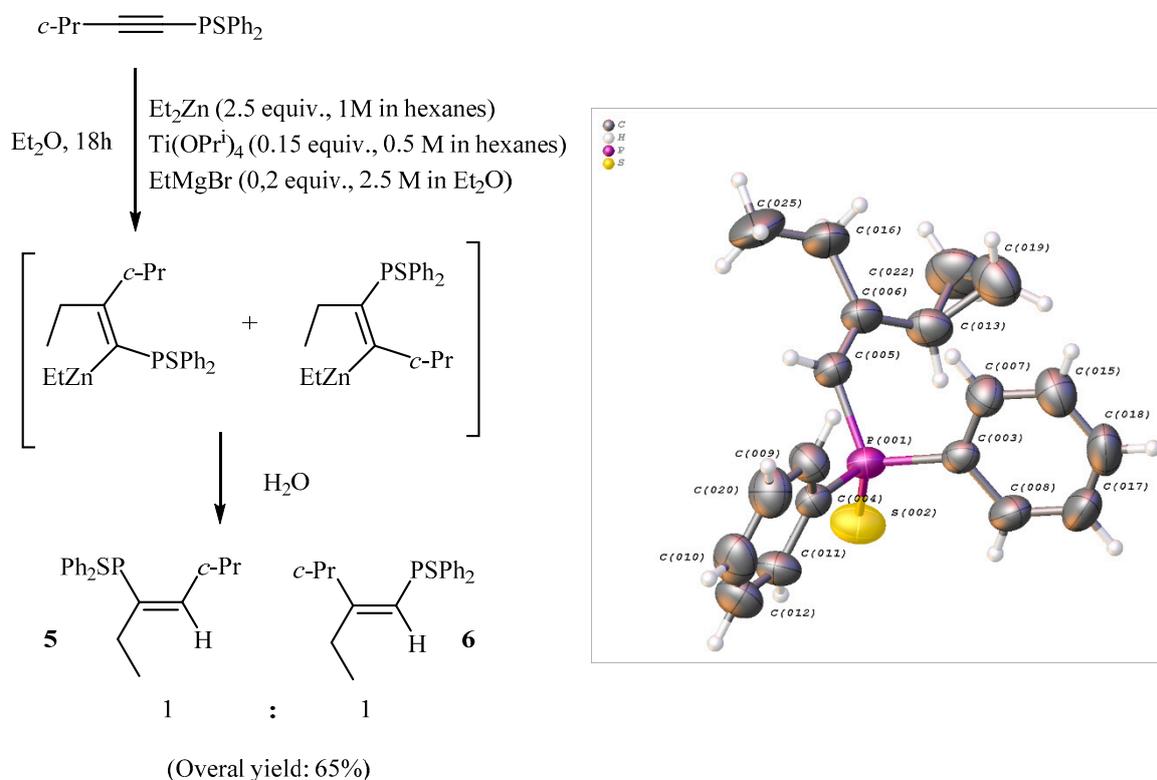


Figure 3. Ti-Mg-catalyzed carbozincation of substituted (cyclopropylethynyl) diphenylphosphine sulfide with Et_2Zn .

The structure of regioisomer **6** with the geminal location of cyclopropyl and ethyl fragments at the double-bond carbon was defined by X-ray diffraction. Presumably, one of the factors responsible for the observed non-selective transformation of cyclopropyl-substituted alkynylphosphine sulfide is the presence of C–C agostic interaction between the titanium atom and cyclopropane ring. The agostic interaction involving cyclopropane moieties was reported for Pt complexes, such as $[\text{PtCl}_2(c\text{-C}_3\text{H}_6)]_2$ and $\text{PtCl}_2(c\text{-C}_3\text{H}_6)(\text{py})_2$ (py = pyridine) [17], and for lithium cyclopropoxide complex [18,19].

Thus, depending on the substituent, Ti-Mg-catalyzed reaction of functionally substituted alkynes with Et_2Zn follows either a 2-zincoethylzincation (1-alkynylphosphines, 2-alkynylamines) [1] or ethylzincation (1-alkynylphosphine sulfides) pathway. In this respect, it was interesting to study the behavior of acetylenic alcohols and ethers in this reaction. Unfortunately, our attempts to perform this reaction with hept-2-yn-1-ol, oct-3-yn-1-ol, or (hept-2-yn-1-yloxy) benzene in diethyl ether failed. Probably, coordination of the titanium ethylene complex (which can be represented as an equivalent of divalent $\text{Ti}(\text{O-}i\text{Pr})_2$ stabilized by ethylene ligand [20]) to the oxygen atom of phosphine oxide, alcohol, or ether group gives a stable unreactive organometallic complex. This complex formation inhibits titanium coordination to the triple carbon–carbon bond and thus prevents the formation of titanacyclopentene.

2.2. The EtMgBr and $\text{Ti}(\text{O-}i\text{Pr})_4$ -Catalyzed 2-Zincoethylzincation of Substituted Substituted Propargylamines with Et_2Zn

In view of the presumed importance of various ligand coordination effects for this reaction, we studied the EtMgBr and $\text{Ti}(\text{O-}i\text{Pr})_4$ -catalyzed reaction of substituted propargylamines with Et_2Zn in solvents of different nature. The reaction of *N,N*-dimethylbut-2-ynyl-1-amine **7a** with 2.5 equivalents of Et_2Zn (1 M in hexane) in the presence of 0.15 equivalent of $\text{Ti}(\text{O-}i\text{Pr})_4$ (0.3 M in hexane) and 0.2 equivalent of EtMgBr (2.5 M in Et_2O) was equally efficient in diethyl ether, anisole, dichloromethane, hexane, benzene, or toluene and resulted in regio- and stereoselective formation of dideuterated allylamine **8a** with *Z*-configuration (Figure 4). Similar results were obtained for *N,N*-dimethylundec-2-ynyl-1-amine, 1-(hept-2-yn-1-yl)piperidine, *N,N*-dimethylnon-2-ynyl-1-amine, and 4-(hept-2-yn-1-yl)morpholine. More evidence for the structure of the resulting allylamines was gained by converting them to iodolysis products **10c** and **10e**. Meanwhile, *N,N*-dimethylbut-2-ynyl-1-amine **7a** proved to be completely inert towards the reaction carried out in 1,4-dioxane, tetrahydrofuran, 1,2-dichloroethane, 1,2-dimethoxyethane, chloroform, or triethylamine.

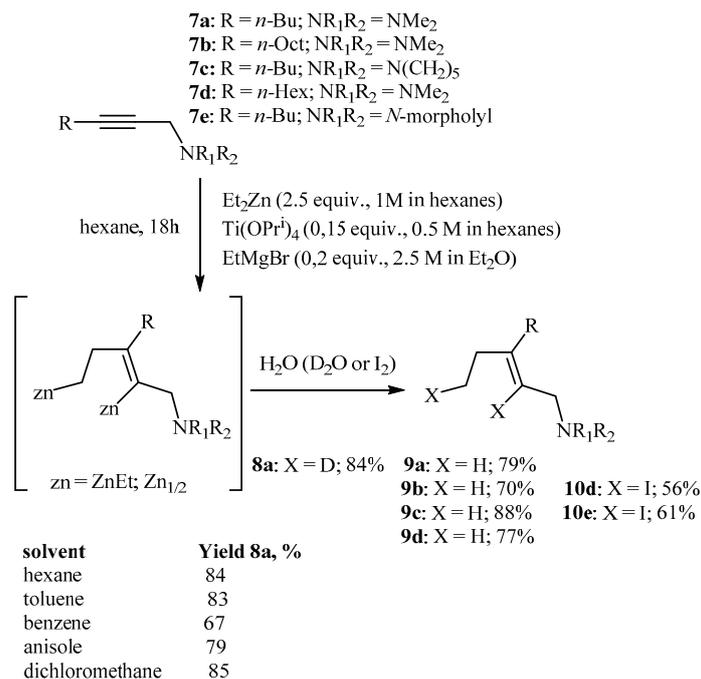


Figure 4. EtMgBr and Ti(O-*i*Pr)₄-catalyzed 2-zincoethylzincation of substituted propargylamines with diethylzinc in various solvents.

We suggested that in the case of 1,2-dimethoxyethane, 1,4-dioxane, tetrahydrofuran, and triethylamine, the acetylenic substrate molecule cannot displace the solvent molecule from the coordination sphere of the low-valence titanium atom in intermediate **E** (Figure 5) and, hence, intermediate **F** is not formed and the catalytic cycle is interrupted. Quantum chemical B3LYP/6-31G(d,p) modeling of the step of displacement of a solvent molecule by *N,N*-dimethylbut-2-ynyl-1-amine, which was chosen as the model compound, demonstrated that the ease of displacement (Gibbs free energy) increases in the series Et₃N (−3.1 kcal/mol) < THF (−4.9 kcal/mol) < Me₂O (−6.5 kcal/mol). According to quantum chemical calculations, for dichloromethane, hexane, or aromatic hydrocarbons (benzene, toluene) as solvents, the equilibrium between intermediates **A** and **E** is shifted towards the non-solvated titanacyclopropane **A**, which facilitates the formation of intermediate **F**.

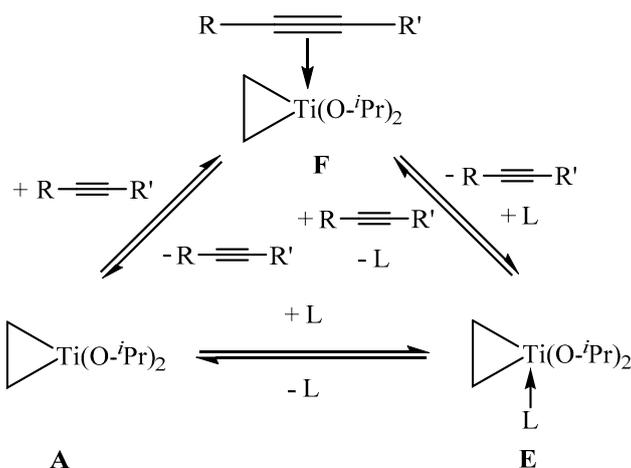


Figure 5. Ligand exchange in the coordination sphere of the titanium atom of titanacyclopropane intermediate.

Despite similar natures of dichloromethane, 1,2-dichloroethane, and chloroform, the reaction smoothly proceeds in dichloromethane, but does not take place in 1,2-dichloroethane or chloroform.

In our opinion, this difference may be attributable to the instability of chloroform and 1,2-dichloroethane under conditions of reaction with EtMgBr and Ti(O-*i*Pr)₄. The use of these solvents in organomagnesium chemistry is fairly limited. For instance, it is known that phenylmagnesium bromide and ethylmagnesium iodide readily react with chloroform and tetrachloromethane to give dihalocarbenes [21]. On the other hand, there are many examples of cross-coupling reactions of Grignard reagents with polychlorinated solvents activated by transition metal catalysts [22–26].

2.3. EtMgBr and Ti(O-*i*Pr)₄-Catalyzed 2-Zincoethylzincation of Substituted 1-Alkynylphosphines with Diethylzinc

In connection with the obtained results, we were interested in studying the effect of various solvents on the EtMgBr and Ti(O-*i*Pr)₄-catalyzed reaction of *P*-containing alkynes—1-alkynylphosphines, 1-alkynylphosphine sulfides, and 1-alkynylphosphine oxides with Et₂Zn. The reaction of substituted 1-alkynylphosphines **11** with 2.5 equivalents Et₂Zn (1 M in hexanes) in the presence of 0.15 equivalent Ti(O-*i*Pr)₄ (0.3 M in hexanes) and 0.2 equivalent EtMgBr (2.5 M in Et₂O) at room temperature followed by oxidation with an aqueous solution of H₂O₂ (37%) or sulfuration with elemental sulfur is equally effective in diethyl ether [1], methylene chloride, hexane, and toluene with regio- and stereoselective formation of the corresponding 1-alkenylphosphine oxides and sulfides of the *Z*-configuration **12a**, **13b,c** and **14c** (Figure 6).

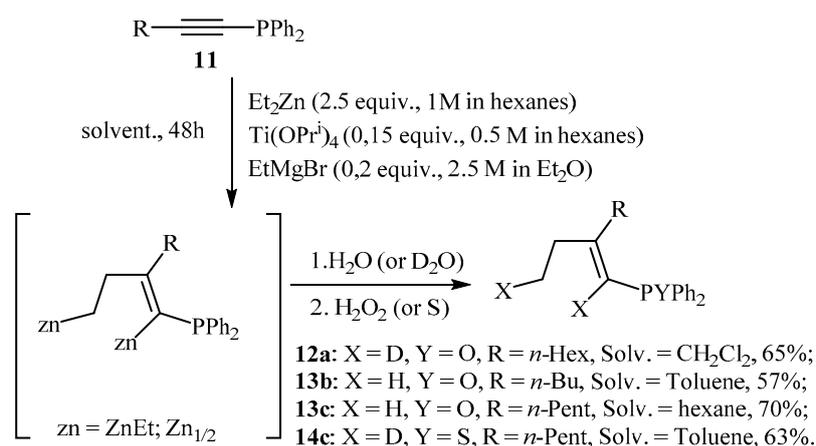


Figure 6. Ti-Mg-catalyzed carbozincation of substituted 1-alkynylphosphines with Et₂Zn in various solvents.

It should be noted that for the complete conversion of 1-alkynylphosphines **11** at room temperature in methylene chloride, toluene, and hexane, about 48 h are required. An increase in temperature to 40 °C leads to a deterioration in the selectivity of the reaction and the formation of difficult-to-analyze mixture of products. As expected, hept-1-yn-1-yl-diphenylphosphine oxide was inert not only in diethyl ether (as described above) but also in methylene chloride, toluene, and hexane. At the same time, the Ti-Mg-catalyzed reaction of substituted 1-alkynylphosphine sulfides with Et₂Zn in methylene chloride, toluene, and hexane does not proceed stereoselectively and leads to the formation of a mixture of stereoisomers. For example, the reaction of hept-1-yn-1-yl-diphenylphosphine sulfide **15** with 2.5 equiv. Et₂Zn (1 M in hexanes) in the presence of 15 mol. % Ti(O-*i*Pr)₄ (0.3 M in hexanes) and 20 mol. % EtMgBr (2.5 M in Et₂O) in methylene chloride leads to the formation of a mixture of **16** (*Z*)- and **17** (*E*)-isomers in a 2:1 ratio with a total yield of 71% (Figure 7).

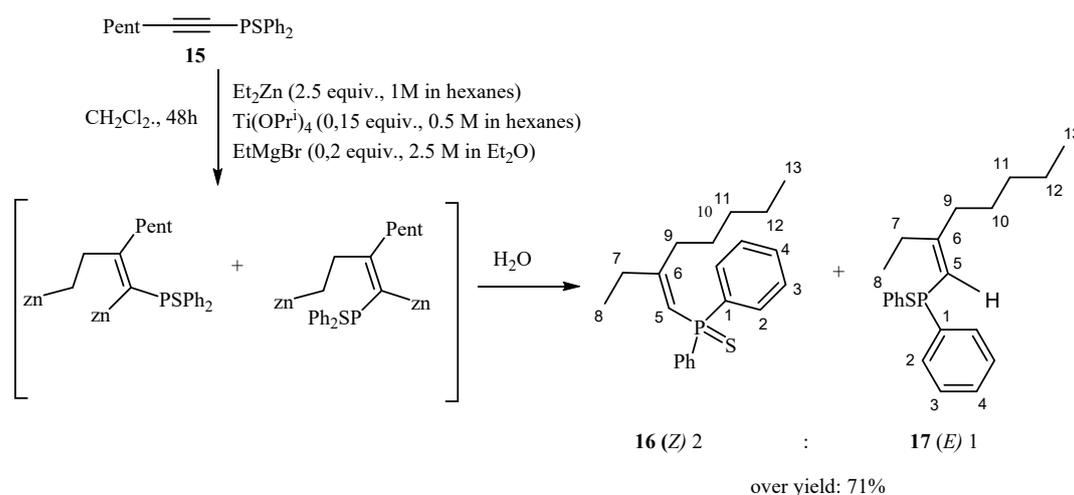


Figure 7. Ti-Mg-catalyzed carbозincation of substituted hept-1-yn-1-yl-diphenylphosphine sulfide.

The formation of an isomeric mixture is indicated in the ¹³C NMR spectrum of the reaction products by the presence of a double set of signals in a 2:1 ratio of the following carbon atoms: C-6 (δ 168.3 ppm and δ 168.1 ppm), C-7 (δ 31.2 ppm and δ 27.1 ppm), C-8 (δ 12.2 ppm and δ 11.5 ppm), C-9 (δ 34.2 ppm and δ 37.9 ppm), C-10 (δ 27.1 ppm and δ 27.5 ppm), C-11 (δ 31.9 ppm and δ 31.6 ppm), C-12 (δ 22.4 ppm and δ 22.5 ppm), C-13 (δ 13.9 ppm and δ 14.1 ppm). The Overhauser effects observed in the NOESY spectrum between the methylene group H₂C-9 (δ 2.39 ppm) and the protons of the aromatic substituent of the compound **16**, as well as the cross-interaction between the protons H₂C-7 (δ 2.27 ppm) and HC-5 (δ 6.03 ppm) of the compound **17** allowed us to identify the obtained adducts as *Z*- and *E*-isomers, respectively.

3. Materials and Methods

3.1. Materials

The reagents were obtained from Acros and Sigma-Aldrich. Hexane and dichloromethane were dried over P₂O₅. 1,4-Dioxane, diethyl ether, tetrahydrofuran, toluene, benzene, and anisole were dried over sodium. Dried 1,2-dimethoxyethane was obtained from Sigma-Aldrich. 1-Alkynyl derivatives of phosphine oxides and 1-alkynyl phosphine sulfides **1** were prepared by the oxidation of 1-alkynyl phosphines with 30% aq. H₂O₂ [27] and based on the reaction of 1-alkynyl phosphines with sulfur [28], respectively. 1-Alkynylamines **7a**, **7b**, and **7d** were synthesized by aminomethylation of terminal alkynes by bisamine [29]. Alkynylamines **7c** and **7e** were prepared by aminomethylation of terminal alkynes with aqueous formaldehyde, 37 wt. % in H₂O and secondary amines using a CuI catalysis [30]. Nuclear magnetic resonance spectroscopy was performed. NMR spectra were recorded on a Bruker Avance 400 spectrometer at 400 MHz for ¹H and at 100 MHz for ¹³C in CDCl₃. The numbering of atoms in the ¹H and ¹³C NMR spectra of the compounds **3a–c**, **4a**, **5**, **6**, **8a**, **9a–d**, **10d**, **10e**, **12a**, **13b,c**, **14c**, **16**, **17** is shown in the Supplementary Materials. X-ray diffraction analysis was performed with an XCaliburEos diffractometer (graphite monochromator, MoKα radiation, λ = 0.71073 Å, w-scan mode, 2θmax = 62°). The data were treated using the CrysAlisProOxfordDiffractionLtd. program package, version 1.171.36.20. The refinement was done with the SHELX97 program package [31]. Elemental analysis was implemented with a Carlo-Erba CHN 1106 elemental analyzer. Mass spectra were obtained using a Finnigan 4021 instrument. The yields of chemical reaction products were obtained from the isolated amount of 2-alkenyl amines, 1-alkenyl phosphine oxides, and 1-alkenyl phosphine sulfides obtained from starting alkynes. All quantumchemical calculations were carried out using the B3LYP/6-31G(d,p) basis set (Gaussian 09 software) [32]. The ¹³C NMR and ¹H NMR data of the products are shown in the Supplementary Materials.

3.2. Methods

3.2.1. Preparation of 1-Alkenyl Phosphine Sulfides **3a–c**, **4a** and **5**, **6** via Ethylmagnesium Bromide and Titanium(IV) Isopropoxide-Catalyzed Reaction of 1-Alkynyl Phosphine Sulfides with Et₂Zn

(Z)-(2-Ethylhex-1-en-1-yl)diphenylphosphine sulfide (**3a**). Typical Procedure. To a solution of hex-1-yn-1-ylidiphenylphosphine sulfide (596 mg, 2 mmol) and Et₂Zn (1 M in hexanes, 5 mL, 5 mmol) in ether (6 mL) was added Ti(O-*i*Pr)₄ (0.5 M in hexanes, 0.6 mL, 0.3 mmol). Ethylmagnesium bromide (2.5 M in Et₂O, 0.16 mL, 0.4 mmol) was then added dropwise, and the reaction mixture turned black. After 18 h at room temperature, the mixture was diluted with Et₂O (5 mL), and 25 wt % aq. KOH (3 mL) was added dropwise while the flask was cooled in an ice bath. The aqueous phase was extracted with Et₂O (3 × 5 mL). The combined organic phase was washed with a saturated aqueous solution of NaCl (10 mL) and dried over anhydrous MgSO₄. The reaction mixture was filtered and concentrated in vacuo to give the crude product as a yellow oil. Evaporation of the solvent and purification of the residue by column chromatography (hexane:ethyl acetate:methanol = 5:2:1) gave **3a** (538 mg, 82%) as a colorless oil. *R*_f 0.42. ¹H NMR (δ, ppm, J/Hz): 0.73 (t, *J* = 7.3, 3H, C(12)H₃), 1.00–1.10 (m, 2H, C(11)H₂), 1.13 (t, *J* = 7.4, 2H, C(8)H₃), 1.20–1.30 (m, 2H, C(10)H₂), 2.29 (q, *J* = 7.5, 2H, C(7)H₂), 2.37 (t, *J* = 7.4, 2H, C(9)H₂), 6.03 (d, *J* = 23.5, 2H, C(7)H₂), 7.25–8.00 (m, 10H, Ph). ¹³C NMR (δ, ppm, J/Hz): 12.17 (C(8)), 13.79 (C(12)), 22.80 (C(11)), 29.48 (C(10)), 31.21 (d, *J* = 16.4, C(7)), 33.92 (d, *J* = 9.3, C(9)), 115.99 (d, *J* = 89.4, C(5)), 128.43 (d, *J* = 12.3, 4C, C(3)), 131.01 (d, *J* = 2.5, 2C, C(4)), 131.20 (d, *J* = 10.5, 4C, C(2)), 135.21 (d, *J* = 84.2, 2C, C(1)), 168.22 (C(6)). ³¹P NMR (δ, ppm): 28.68. MS (EI): *m/z*, % = 328 (45) [M⁺], 299 (18), 254 (4), 218 (100), 183 (48), 139 (30), 108 (18), 41 (17). Anal. calcd for C₂₀H₂₅PS, (%): C, 73.14; H, 7.67. Found, %: C, 73.20; H, 7.71. The ¹H NMR and ¹³C NMR of the compounds **3b,c**, **4a**, **5**, **6** data of coupling products were shown in the Supplementary Materials.

3.2.2. Preparation of 1-Alkenyl Phosphine Oxides **12a**, **13b**, **13c**, **14c**, **16**, and **17** via Titanium(IV) Isopropoxide and Ethylmagnesium Bromide-Catalyzed Reaction of 1-Alkynyl Phosphines with Et₂Zn

(Z)-(2-(Ethyl-2-d)oct-1-en-1-yl-1-d)diphenylphosphine oxide (**12a**). Typical Procedure. To a solution of oct-1-yn-1-ylidiphenylphosphane (588 mg, 2 mmol) and Et₂Zn (1 M in hexanes, 5 mL, 5 mmol) in dichloromethane (5 mL) was added Ti(OPr-*i*)₄ (0.5 M in hexanes, 0.6 mL, 0.3 mmol). Ether solution of EtMgBr (2.5 M in Et₂O, 0.16 mL, 0.4 mmol) was then added, and the mixture turned black. After 48 h at room temperature, CH₂Cl₂ (5 mL) was added to the reaction mixture, and D₂O (3 mL) was added dropwise while the flask was cooled in an ice bath. The aqueous inorganic layer was extracted through CH₂Cl₂ (3 × 5 mL). The combined organic phase was washed sequentially with water and brine (10 mL) and dried over anhydrous MgSO₄. The solvent was evaporated under reduced pressure. A 30% hydrogen peroxide solution (0.35 mL, 3 mmol) was slowly added dropwise with vigorous stirring to a solution of the crude residue (2-(Ethyl-2-d)oct-1-en-1-yl-1-d)diphenylphosphine oxide, in chloroform (5 mL). The reaction mixture was stirred for 1 h and washed with water (3 × 5 mL), the organic layer was dried over MgSO₄. The reaction mixture was filtered through a filter paper and concentrated in vacuo to give crude product as a yellow oil that was purified by column chromatography (silica gel, hexane:ethyl acetate:methanol = 5:2:1) to afford **12a** (445 mg, 65%). *R*_f 0.59. The spectral properties (¹H NMR, ¹³C NMR, MS) were in good agreement with those that were reported in the literature [33]. The ¹H NMR and ¹³C NMR of the compounds **13b**, **13c**, **14c**, **16**, **17** data of coupling products are shown in the Supplementary Materials.

3.2.3. Preparation of Allylic Amines **8a**, **9a–d** via Titanium(IV) Isopropoxide and Ethylmagnesium Bromide-Catalyzed Reaction of 2-Alkynylamines with Et₂Zn

(Z)-3-(Ethyl-2-d)-*N,N*-dimethylhept-2-en-1-amine-2-d (**8a**). Typical Procedure. To 278 mg of *N,N*-dimethylhept-2-yn-1-amine (2 mmol) and 5 mL of Et₂Zn (1 M in hexanes, 5 mmol) suspended in 6 mL hexane was added under an atmosphere of argon Ti(OPr-*i*)₄ (0.5 M in hexanes, 0.6 mL, 0.3 mmol). Then sequentially, EtMgBr (2.5 M in Et₂O, 0.16 mL, 0.4 mmol) was added, and the mixture turned

black. After 18 h at room temperature, the reaction mixture was diluted with Et₂O (5 mL), and D₂O (3 mL) was added dropwise while the flask was cooled in an ice bath. The aqueous layer was extracted with Et₂O (3 × 5 mL). The organic layers were washed with brine (10 mL), dried over anhydrous CaCl₂. The reaction mixture was filtered through a filter paper and concentrated in vacuo to give crude product as a yellow oil. The residue was distilled through a micro column at 10 mmHg to give 8a (287 mg, 84%) as a colorless oil. b.p. 87–89 °C (10 mmHg) (lit. ⁷ b.p. 91–93 °C (15 mmHg)). ¹H NMR (400MHz, CDCl₃): δ = 0.92 (t, *J* = 6.3 Hz, 3H, C(11)H₃), 1.00 (t, *J* = 7.7 Hz, 3H, C(5)H₃), 1.25–1.40 (m, 4H, C(9,10)H₂), 2.03 (t, *J* = 7.8 Hz, 2H, C(4)H₂), 2.10–2.35 (m, 2H, C(8)H₂), 2.23 (s, 6H, C(6,7)H₃), 2.90 (s, 2H, C(1)H₂). ¹³C NMR (100 MHz, CDCl₃): δ = 12.41 (t, C(5), ¹*J*_{CD} = 19.3 Hz), 14.02 (C(11)), 22.84 (C(10)), 29.41 and 30.30 and 30.71 (C(4,8,9)), 45.26 (2C(6,7)), 56.77 (C(1)), 144.27 (C(3)).

MS (EI): *m/z*, % = 171 (14) [M⁺], 142 (10), 126 (18), 112 (21), 95 (100), 82 (32), 58 (49), 46 (48). Anal. calcd for C₁₁H₂₁D₂N, (%): C, 77.12. Found, %: C, 77.21. The ¹H NMR and ¹³C NMR of the compounds 9a–d data of coupling products are shown in the Supplementary Materials.

3.2.4. The Iodination of Intermediate Organozinc Compounds

(*Z*)-2-Iodo-3-(2-iodoethyl)-*N,N*-dimethylnon-2-en-1-amine (**10d**). Typical Procedure. To a solution of *N,N*-dimethylnon-2-yn-1-amine (334 g, 2 mmol) and Et₂Zn (1 M in hexanes, 5 mL, 5 mmol) in toluene (6 mL) was added Ti(OPr-*i*)₄ (0.5 M in hexanes, 0.3 mL, 0.2 mmol) followed by ethylmagnesium bromide (2.5 M in Et₂O, 0.16 mL, 0.4 mmol). After 18 h at 23 °C, the reaction mixture was cooled to –78 °C, and a solution of I₂ (1575 mg, 12.5 mmol) in THF (12.5 mL) was added via cannula. The mixture was warmed to room temperature and stirred for 10 h. The mixture was then treated by a 25% water solution of KOH and Et₂O. The organic phase was washed with water and an aqueous solution of Na₂S₂O₃, drying with MgSO₄. Evaporation of the solvent and purification of the residue by column chromatography (hexane/ethyl acetate, 5:1) gave a yellow oil; yield: 503 mg, (56%); *R*_f = 0.73 (hexane/ethyl acetate, 5:1). The spectral properties (¹H NMR, ¹³C NMR, MS) of the compounds **10d**, **10e** were in good agreement with those that were reported in the literature [1].

4. Conclusions

Thus, Ti-Mg-catalyzed carbozincation of 1-alkynylphosphine sulfides with Et₂Zn in a solution of diethyl ether proceeds in a stereoselective manner, while the use of methylene chloride, hexane, and toluene as solvents leads to the formation of a mixture of stereoisomers. In the present work, it was also demonstrated that the selective Ti-Mg-catalyzed 2-zincethylzincation of 2-alkynylamines and 1-alkynylphosphines is possible not only in diethyl ether, as we showed earlier [1], but also in such solvents as hexane, methylene, benzene, toluene, and anisole. This study opens up further prospects for the use of metal complex catalyzed organozinc synthesis to create new methods for the production of olefins based on various transformations of functionalized acetylene derivatives.

Supplementary Materials: The following are available online at <http://www.mdpi.com/2073-4344/9/12/1022/s1>, analytical data and NMR spectrum for all compounds.

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