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Catalytic Addition of *O*-Methyl (Adamant-2-ylmethyl)phosphonite to Phenylacetylene

A. N. Reznikov and Yu. N. Klimochkin

Samara State Technical University, ul. Molodogvardeiskaya 244, Samara, 443100 Russia
e-mail: orgphosphorus@yandex.ru

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Abstract—The catalytic addition of *O*-methyl (adamant-2-ylmethyl)phosphonite to phenylacetylene in the presence of complexes of Pd, Cu, and Ni was studied. Pd(0)-Catalyzed addition led to the preferential formation of the Markovnikov's adduct. Copper and nickel complexes exhibit low catalytic activity in the reaction. Effect of the catalyst nature and modifying additives on chemo- and regioselectivity of the reaction was discussed.

Keywords: hydrophosphorylation, *H*-phosponites, alkynes, metal complex catalysis

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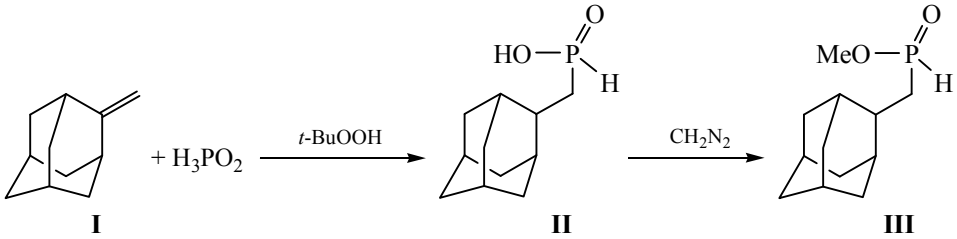
Addition of the molecules containing H–P bond to alkynes is a convenient and effective approach towards the synthesis of α,β-unsaturated organophosphorus compounds used in organic synthesis [1–6], medicine [7, 8] and as promising ligands for metal complex catalysis [9–11]. The use of transition metal complexes as catalysts allows performing these reactions with high regio- and stereoselectivity.

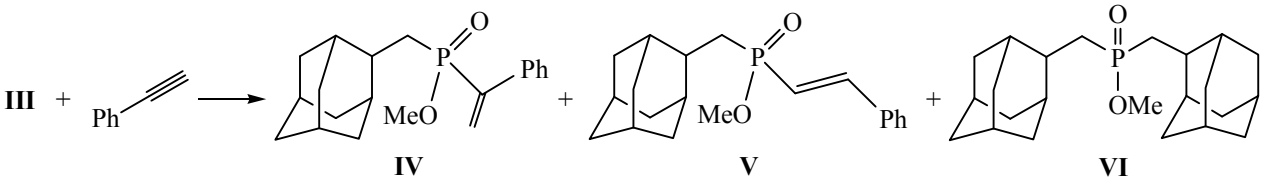
Catalytic hydrophosphorylation of alkynes has been first reported in [12]. To date, the addition of secondary phosphites and phosphine oxides to alkynes [13] affording alkenylphosphonates and alkenylphosphine oxides, respectively, are the most studied reactions. In a number of researches a wide range of unsaturated substrates and hydrophosphoryl compounds, and also the possibility of changing the regioselectivity of the reaction by modifying the catalyst was explored [14, 15]. Despite the large amount of publications in this area, there are certain unsolved problems related to the selectivity and the influence of the nature of the substituents in the molecules of hydrophosphoryl compounds. In general, the regioselectivity of the catalytic addition of hydrophosphoryl compounds and secondary phosphines to alkynes is determined by the reaction mechanism: in the case of insertion of the alkyne in the Pd–H bond the Markovnikov's adduct formed, while the insertion of the alkyne in the Pd–P bond led to the formation of the adducts against the Markovnikov's rule [16]. Theoretical calculations show that in the first case the adduct forms readily under the kinetic control and in the second case the adduct may be formed under the thermodynamic control. Among the Pd complexes when passing from the secondary phosphines to phosphites the formation of the adducts due to the insertion in the Pd–P bond becomes more likely [16, 17]. Phosponites by their reactivity should occupy an intermediate position between phosphines and phosphites.

The catalytic addition of monoalkylphosphonites to alkynes has been poorly investigated. In the literature there are reports on the addition of *O*-ethylphenylphosphonite to phenylacetylene in the presence of Pd(0) complexes generated from palladium(II) acetate and phosphine ligands. When tris(*tert*-butyl)phosphine was used, the adduct was formed against the Markovnikov's rule, whereas the use of 1,2-bis(diphenylphosphino)-ethane led to the formation of the Markovnikov's adduct [18]. Addition of *O*-ethylphenylphosphonite to phenylacetylene was also possible in the presence of Ni(0) complexes with methyldiphenylphosphine and dimethylphenylphosphine [14]. In the latter case the phosphine complex was generated from $[Ni(cod)_2]$, and addition of diphenylphosphinic acid can improve the reaction regioselectivity. The successful use of the

Scheme 1.



Scheme 2.



catalyst system CuI/1,2-ethylene diamine in the reaction of *O*-ethylphenylphosphonite with phenylacetylene has been reported in [19]. The reaction proceeded in dimethyl sulfoxide to afford the anti-Markovnikov adduct in a high yield. Using the Pd, Ni, and Cu complexes as an example, the influence of the metal nature on the reaction regioselectivity was shown, but all the studies were limited by using *O*-ethylphenylphosphonite as the hydrophosphoryl reagent. Reactions with phosphonites containing aliphatic and alicyclic substituents have not been studied.

At the same time, an important question remains about the influence of the substituents at the phosphorus atom on addition of phosphonites to alkynes. To elucidate the role of the steric factors on the reactivity of phosphonites and the reaction regioselectivity, we prepared *O*-methyl (adamant-2-yl-methyl)phosphonite and studied its interaction with phenylacetylene in the presence of palladium, nickel, and copper complexes.

O-Methyl (adamant-2-ylmethyl)phosphonite **III** was prepared by reacting methyleneadamantane **I** and hypophosphorous acid under the radical initiation conditions followed by treating the phosphonous acid **II** with diazomethane (Scheme 1).

The reaction of phosphonite **III** with phenylacetylene in the presence of Pd(0) complexes was carried out in THF at various temperatures and a ratio of catalyst:substrate = 3 : 100.

Complexes $[Pd(Ph_3P)_4]$ and $[Pd(Ph_3P)_2]$, generated in situ from $[PdCl_2(Ph_3P)_2]$, and diisobutylaluminum hydride (DIBAL-H) [20] were used as catalysts. The reaction progress was monitored by gas chromatography-mass spectrometry.

When $[Pd(Ph_3P)_4]$ complex was used, complete conversion of phosphonite **III** was achieved in 15 h at 90°C; methyl bis(adamant-2-ylmethyl)phosphinate **VI** was formed as a byproduct. The addition of hydrophosphoryl compound occurred mainly at the α-position to give the corresponding 1-phenylethenylphosphinate **IV**, whose structure was confirmed by ^1H and ^{13}C NMR spectroscopy (Scheme 2).

In addition, the β-adduct **V** was also formed. According to gas chromatography-mass spectrometry, the ratio of isomers in the reaction mixture was 6.1 : 1. The application of the catalytic system $[PdCl_2(Ph_3P)_2]$/DIBAL-H caused some decrease in the reaction regioselectivity (**IV** : **V** = 4.9 : 1), but in this case there was no disproportionation product formation even at high reaction temperature (110°C).

Ananikov et al. [21] noted an increase in the product yield and in the selectivity of the reaction of alkynes with dialkyl phosphites at the use of the catalytic system [Pd]/CF_3COOH. As they suggested, the beneficial effect of trifluoroacetic acid consisted in shifting the equilibrium between the various forms of phosphite complexes of palladium towards the active palladium hydride form, which accelerated the reaction and increased the yield. To determine the effect of modifying acid additive on the reaction regioselectivity, we performed the reaction of phosphonite **III** with phenylacetylene in the presence of $[Pd(Ph_3P)_4]$ and trifluoroacetic acid. The catalyst modification

Reaction of phosphonite **III** with phenylacetylene in the presence of metals complexes[a]

Catalyst	Solvent	Temperature, °C	Conversion of phosphonite, %[b]	Yields of the reaction products, %[b]		
				IV	**V**	**VI**
$[Pd(Ph_3P)_4]$	THF	67	25.5	14.6	–	10.9
$[Pd(Ph_3P)_4]$	THF	90	100	77.4	12.6	10.0
$[Pd(Ph_3P)_4]/CF_3COOH$[c]	THF	90	100	79.2	5.4	15.4
$[PdCl_2(Ph_3P)_2]$/DIBAL-H[d]	THF	110	100	83.1	16.9	–
CuI/eda[e]	DMSO	110	100	14.8	9.9	75.3
$[CuI(Ph_3P)]_2$	DMSO	110	6.8	1.2	–	5.6
$[NiCl_2(PPh_3)_2]/Et_2Zn$[d]	THF	110	6.1	–	–	6.1

[a] Reaction conditions: 3 mol % of the catalyst, 1.40 mmol of phosphonite **III**, 1.40 mmol of phenylacetylene, 2.2 mL of the solvent, 15 h.
[b] According to gas chromatography-mass spectrometry. [c] Molar ratio was 3 : 2. [d] Molar ratio was 1 : 3. [e] Molar ratio was 1 : 1.5.

resulted in a significant increase in the reaction regioselectivity (**IV** : **V** = 14.6 : 1) and also in the yield of **VI**.

Using the catalytic system CuI/1,2-ethylene diamine in the reaction of phosphonite **III** with phenylacetylene led to the preferential formation of compound **VI**. Addition of phosphonite **III** to the alkyne occurred non-selectively. The total yield of the isomeric adducts **IV** and **V** was 24.7%. The binuclear copper complex with triphenylphosphine was virtually inactive in the reaction.

The formation of *O*-methyl bis(adamant-2-yl)phosphinate **VI** as a byproduct was probably due to the occurrence of a radical dephosphorylation of the source phosphonite in the presence of transition metals. Alkylphosphonic acid is known to undergo dephosphorylation in the presence of $Cu(OAc)_2/Pb(OAc)_4$; yields of the corresponding alkenes increases when passing from linear to branched alkyl substituents (corresponding to an increase in the radical stability) [22]. By analogy with the suggested mechanism of dephosphorylation of alkylphosphonic acids [22], we assumed that in the first stage Cu(I) salt of phosphonite **III** forms, from which adamantylmethyl radical is generated. This radical attacks the second phosphonite molecule leading to the formation of phosphinate **VI**.

EXPERIMENTAL

Elemental analysis was performed on an EuroVector EA 3000 analyzer. NMR spectra were recorded on a Jeol JNM-ECX400 [399.78 (^{1}H) and 100.53 MHz (^{13}C)] using $CDCl_3$ as solvent. Mass spectra were obtained on a Finnigan Trace DCQ gas chromatograph-mass spectrometer using a capillary column BPX-5 (30 × 0.32, SGE) at the energy of ionizing electrons of 70 eV. Flash chromatography was performed using Kieselgel 60 (0.04–0.063 μm) eluting with methylene chloride.

(Adamant-2-ylmethyl)phosphonous acid (II). A mixture of 2.41 g (36.5 mmol) of hypophosphorous acid in 2.4 mL of water and 4.5 g (30.4 mmol) of 2-methyleneadamantane **I** in 19 mL of isopropanol was heated to reflux. Then a solution of 0.19 mL of 70% aqueous *tert*-butyl hydroperoxide in 5.5 mL of isopropanol was added by portions within 2 h. After the solvent was removed, the reaction mixture was treated with 30% aqueous potassium hydroxide solution to pH 9, and filtered. The filtrate was extracted with toluene, the aqueous phase was separated and acidified with concentrated hydrochloric acid to pH 3. The precipitated phosphonous acid was filtered off, washed with water, and dried. Yield 3.19 g (49.0%), mp 130–132°C. ^{1}H NMR spectrum, δ, ppm: 1.55–1.98 m (14H, Ad; 2H, PCH_2Ad), 2.12–2.30 m (1H, Ad), 7.10 d (1H, PH, $^1J_{HP}$ 560 Hz), 12.35 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 27.74 (CH_2, Ad), 31.50 (CH_2, Ad), 33.17 d (CH, Ad, $^2J_{CP}$ 7.5 Hz), 33.64 d (PCH_2, $^1J_{CP}$ 80.0 Hz), 38.30 (CH, Ad), 39.06 (CH, Ad). ^{31}P NMR spectrum: δ_P 38.51 ppm. Found, %: C 61.59; H 8.90. $C_{11}H_{19}O_2P$. Calculated, %: C 61.67; H 8.94.

***O*-Methyl (adamant-2-ylmethyl)phosphonite (III).** A mixture of 0.68 g (3.18 mmol) of phosphonous acid

and 30 mL of 5% diazomethane solution in THF was stirred for 10 min and evaporated. Yield 0.72 g (quantitative). ^{1}H NMR spectrum, δ, ppm: 1.52 d (2H, CH_2P, $^2J_{HP}$ 12.0 Hz), 1.65–1.95 m (14H, Ad), 2.20 m (1H, Ad), 3.72 d (3H, CH_3O, $^3J_{HP}$ 8.5 Hz), 7.04 d (1H, PH, $^1J_{HP}$ 527.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 27.64 d (CH_2P, $^1J_{CP}$ 16.3 Hz), 31.27 (CH_2, Ad), 31.29 (CH_2, Ad), 31.72 (CH_2, Ad), 32.78 d (CH, Ad, $^2J_{CP}$ 7.6 Hz), 32.82 (CH, Ad), 37.72 (CH, Ad), 38.07 (CH, Ad), 38.89 (CH, Ad), 52.89 d (CH_3O, $^2J_{CP}$ 7.67 Hz). ^{31}P NMR spectrum: δ_P 42.84 ppm. Mass spectrum, *m*/*z* (I_{rel}): 228 (48) $[M]^+$, 207 (14), 149 (100) $[AdCH_2]^+$, 107 (40), 93 (46), 79 (94), 55 (18). M_{calc} 228.27. Found, %: C 63.11; H 9.23. $C_{12}H_{21}O_2P$. Calculated, %: C 63.14; H 9.27.

Reaction of phosphonite III with phenylacetylene. An ampule pre-filled with argon was charged with 0.04 mmol of the catalyst and a solution of 0.32 g (1.40 mmol) of phosphonite and 0.14 g (1.40 mmol) of phenylacetylene in 2.2 mL of THF. The reaction was carried out for 15 h. The reaction mixture was analyzed by gas chromatography-mass spectrometry. The reaction product was isolated by column chromatography.

***O*-Methyl (adamant-2-ylmethyl)(1-phenylethenyl)phosphinate (IV).** ^{1}H NMR spectrum, δ, ppm: 1.49 d (2H, $AdCH_2P$, $^2J_{HP}$ 11.8 Hz), 1.63–1.80 m (2H, Ad), 2.15 m (13H, Ad), 3.72 d (3H, CH_3O, $^3J_{HP}$ 11.0 Hz), 6.17 d.d (1H, =CH, $^2J_{HH}$ 1.8, $^3J_{HP}$ 36.4 Hz), 6.38 d.d (1H, =CH, $^2J_{HH}$ 1.8, $^3J_{HP}$ 19.9 Hz), 7.34–7.42 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 27.64 d ($AdCH_2P$, $^1J_{CP}$ 9.5 Hz), 30.46 (CH_2, Ad), 31.34 (CH_2, Ad), 31.44 (CH_2, Ad), 32.85 d (CH, Ad, $^2J_{CP}$ 9.1 Hz), 38.03 (CH, Ad), 38.81 (CH, Ad), 50.83 d (CH_3O, $^2J_{CP}$ 6.7 Hz), 127.47 d (*o*-CH, Ph, $^3J_{CP}$ 4.8 Hz), 128.80 (*m*-CH, Ph), 132.52 d (=CH_2, $^2J_{CP}$ 6.7 Hz), 137.42 d (*i*-CH, Ph, $^2J_{CP}$ 12.4 Hz), 142.14 d [PC(Ph)=, $^1J_{CP}$ 106.4 Hz]. ^{31}P NMR spectrum: δ_P 46.35 ppm. Mass spectrum, *m*/*z* (I_{rel}): 330 (80) $[M]^+$, 273 (10), 239 (8), 195 (7), 182 (18), 149 (12) $[AdCH_2]^+$, 117 (10), 104 (100), 103 (88), 91 (32), 79 (62), 77 (40), 67 (12). M_{calc} 330.40. Found, %: C 72.64; H 8.20. $C_{20}H_{27}O_2P$. Calculated, %: C 72.70; H 8.24.

***O*-Methyl (adamant-2-ylmethyl)(2-phenylethenyl)phosphinate (V).** Mass spectrum, *m*/*z* (I_{rel}): 330 (60) $[M]^+$, 239 (20), 226 (20), 182 (40), 149 (68) $[AdCH_2]^+$, 148 (48), 133 (12), 117 (22), 105 (22), 91 (36), 79 (62), 77 (36), 67 (12).

***O*-Methyl bis(adamant-2-ylmethyl)phosphinate (VI).** ^{1}H NMR spectrum, δ, ppm: 1.55 m (4H, Ad), 1.70–2.00 m (24H, Ad; 4H, CH_2P), 2.25 m (2H, Ad), 3.68 d (3H, CH_3O, $^3J_{HP}$ 10.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 25.52 (CH, Ad), 27.77 (CH_2, Ad), 31.52 (CH_2, Ad), 33.07 d (CH, Ad, $^2J_{CP}$ 7.5 Hz), 33.60 d (PCH_2, $^1J_{CP}$ 80.0 Hz), 38.31 (CH, Ad), 39.02 (CH_2, Ad), 54.38 d (CH_3O, $^2J_{HP}$ 10.6 Hz). ^{31}P NMR spectrum: δ_P 64.27 ppm. Mass spectrum, *m*/*z* (I_{rel}): 376 (12) $[M]^+$, 228 (100) $[M - AdCH_2]^+$, 149 (86) $[AdCH_2]^+$, 91 (16), 79 (38). M_{calc} 376.51. Found, %: C 73.32; H 9.89. $C_{23}H_{37}O_2P$. Calculated, %: C 73.37; H 9.91.

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