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Interaction of 1,2-alkadienephosphonates with propargyl alcohole

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Abstract*: The reactivity of 1,2-alkadienephosphonates in nucleophilic addition reactions has been investigated.*
Keywords: 1,2-Alkadienephosphonates, nucleophilic addition, β-ketophosphonates

Introduction

The versatile reactivity of 1,2-alkadienephosphonates, allowed them to be used as precursors for synthesis of complex organophosphorus compounds, which often exhibit certain biological activity [1].

Pudovic and co-workers have firstly studied the scope and limitations of 1,2-alkadienephosphonic dialkyl esters in nucleophilic addition reactions [2]. Shortly after, Altenbach and Korff have investigated the same reaction in details [3,4]. The impact of these investigations has been appreciated 23 years later in an in-depth research from Khusainova [5].

Our previous efforts dedicated to this problem [6] together with some relatively recent publication of others [7], motivate us to check the reactivity of certain 1,2-alkadienephosphonates with propargyl alcohol in an $Zn(OTf)_2$ catalyzed nucleophilic addition reaction.

Results and Discussion

Based on literature data, the nucleophilic addition reactions of aliphatic alcohols to 1,2-alkadienephosphonates always need some kind of catalyst involved. In the first report on this subject [2], authors have investigated the addition of ethanol in presence of sodium ethylate as a catalyst. All the next investigations on the subject confirm their results [3-6]. In the recent publication others reported that the reaction of α-alkynoles with the similar 1,2-alkadienephosphonates in an $Zn(OTf)_2$ catalyzed reaction, lead to different and unusual products [7]. Their results provoke us to investigate the reaction between certain 1,2-alkadienephosphonates and propargyl alcohol in presence of $Zn(OTf)_2$ as catalyst, repeating the reaction conditions, described in [7].

The substrates, i.e. dimethyl ester of 1,2-pentadienephosphonic acid **2**, N, N-dialkylamino-O-methyl-1,2-pentadienephosphonic acid **3**, dimethyl-1,2-pentadienephosphine oxide **4** and diphenyl-1,2-pentadienephosphine oxide **5** synthesized by our own procedure (see experimental), have been treated with propargyl alcohol in presence of $Zn(OTf)_2$ and triethylamine in toluene solution, at high temperature for 6 – 10 h and under inert atmosphere. The reactions have been monitored by IR spectral data and TLC. As we expected in all cases with good to excellent yields products **6 -13** of nucleophilic addition of propargyl alcohol to allenyc system have been isolated.
Reaction followed the scheme:

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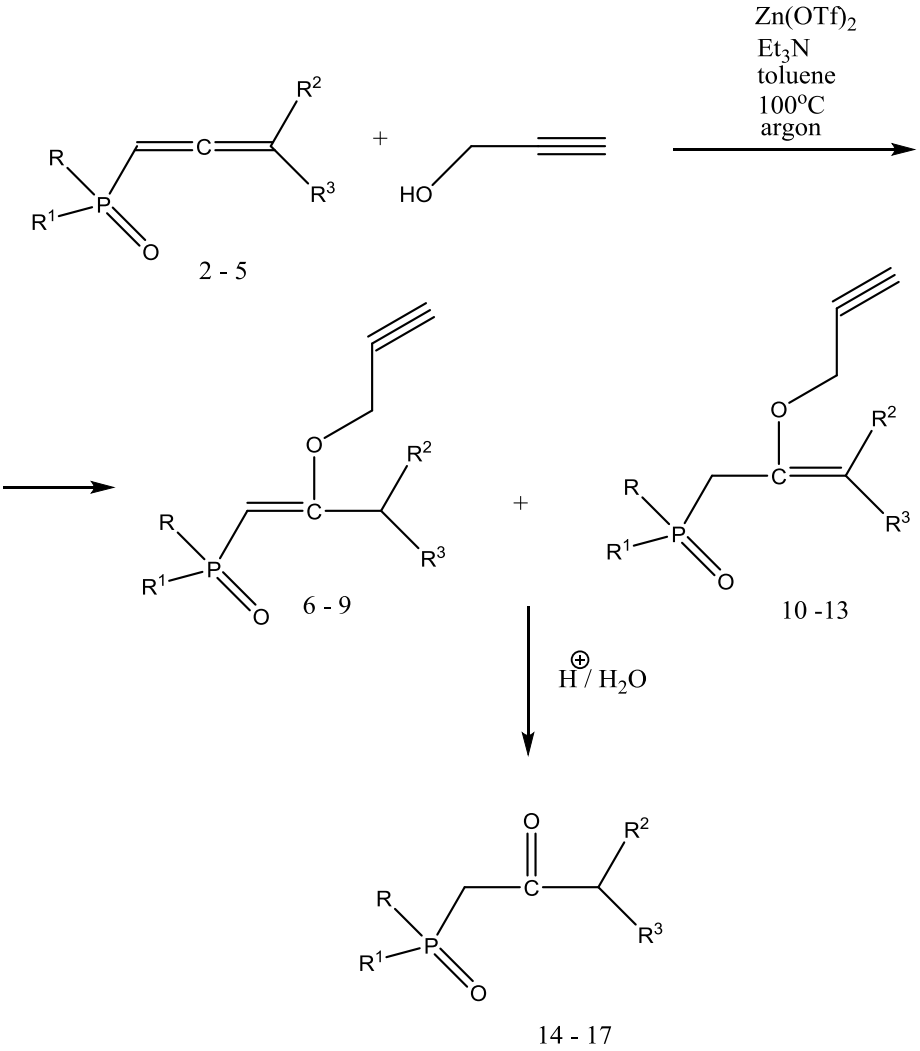

2,6,10,14 R=R[1]=OMe, R[2]=Me, R[3]=Et
3,7,11,15 R=OMe, R[1]=Et_2N, R[2]=Me, R[3]=Et
4,8,12,16 R=R[1]=Me, R[2]=Me, R[3]=Et
5,9,13,17 R=R[1]=Ph, R[2]=Me, R[3]=Et

Shceme 1. Zn(OTf) Catalyzed reaction of 1,2-alkadienephosphonates with propargyl alcohol

The IR investigations of the reaction mixtures obtained by the reaction of compounds 2-5 at the conditions described in [7], show that in all cases the characteristic band for allenic system of double bonds disappears and characteristic band at 1640-1655cm^{-1} appear. The latest confirm the formation of double carbon-carbon bond. On the other hand, irrespective from the reaction time, the characteristic band for a triple carbon-carbon bond at 2000-2012cm^{-1}, presents. All these observations,

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together with the fact that in the first two hours of the reaction an insoluble in the chosen solvent reaction mixtures were formatted, advocated against the proposed reaction mechanism in [7]. Moreover, irrespective from the position of double bond in compounds **6-13**, their hydroxylation in all cases lead to formation of β-ketophosphonates **14-17**. The formation of **14-17** in the latest reaction is a direct evidence for the structure of compounds **6-13**. This results together with the spectral data confirm undoubtful the reaction mechanism, postulated in [3-6].

Experimental

General

All new synthesized compounds were purified by column chromatography and characterized on thr basis of NMR, IR and microanalytical data. NMR spectra were recorded on Brucker Avance II+600(^{1}H at 600.1 MHz, ^{31}P at 242.9MHz) spectrometer in $CDCl_3$ solution. Chemical shifts are in parts per million downfield from internal TMS. *J* values are given in hertz. The IR spectra were run on FT-IRAffinity -1 Shimadzu (Shimadzu Corp., Japan) spectrophotometer. Elemental analyses were carried out by the Microanalytical Service Laboratory of Faculty of Chemistry and Pharmacy, University of Sofia, using Vario EL3 CHNS (O) (Elementar Analysensysteme GmbH, Hanau, Germany). Column chromatography was performed on Kieselgel F_{254}60 (70-230 mesh ASTM, 0.063-0.200 nm, Merck). The solvents were purified by standard methods. All reactions were carried out in oven-dried glassware under an argon atmosphere and exclusion of moisture. All compounds were checked for purity on TLC plates Kieselgel F_{254}60, Merck

General procedure for preparation of 2 and 3

2. To a solution of the corresponding dichloride of 1,2-alkadienephosphonic acid in non-polar media a solution of aliphatic alcohol and base in the same solvent was added under stirring and cooling(-5 to 0^{o}C) for an hour. After standard work-up the residue was purified (hexane: ethylacetate 1:4). [8]

3. To a solution of the corresponding dichloride of 1,2-alkadienephosphonic acid in non-polar media a solution of aliphatic alcohol, diethylamine and base in the same solvent was added under stirring and cooling(-5 to 0^{o}C) for an hour. After standard work-up the residue was purified (hexane: ethylacetate 1:4). [9]

General procedure for preparation of 4 and 5

4. To a solution of the corresponding dichloride of 1,2-alkadienephosphonic acid in non-polar media a solution of Grignard reagent (Mg+MeI) under cooling (-30 to -20^{o}C). After standard work-up the residue was purified (hexane: ethylacetate 1:4). [10]

5. To a solution of corresponding α-acetylenic alcohol in dry methylenechloride at cooling (-20 to -15^{o}C), a mixture from diphenylchlorophosphine and triethylamine dissolved in the same solvent was added. After standard work-up the residue was purified (hexane: ethylacetate 1:4). [11]

General procedure for preparation of 6 - 13

To a solution of **2**, **3**, **4** or **5** in dry toluene a mixture from propargyl alcohol, $Zn(OTf)_2$ and triethylamine, dissolved in the same solvent was added and the resulting reaction mixture was heated up to boiling of the solvent for 6 to 12 h. The reaction was monitored by IR and TLC. After standard work-up the residue was purified (hexane: ethylacetate 2:3). [7]

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General procedure for preparation of 14 -17

To a solution of **6**, **7**, **8**, **9**, **10**, **11**, **12**, or **13** in dry diethyl diethyl ether a 10% HCl was added and the mixture was stirring overnight. After standard work-up the residue was purified (hexane: ethylacetate 1:4). [3]

Compound characterization

14. *Dimethyl(3-methyl-2-oxopentyl)phosphonate,* $C_8H_{17}O_4P$; Calcd.: P 14.88, Found: P 14.66 %; IR: ν(cm^{-1}) 1720 $_{(C=C)}$, 1256 (P=O), 980 (P-O-C), ^{1}H NMR ($CDCl_3$): δ/ppm 3.39(d, $^3J_{HP}$ 10.09Hz, 6H, (OMe)); 3.29(dt, $^2J_{HH}$ 5.8Hz, 1H(C<u>H</u>)); 2.93(d, $^2J_{HP}$ 11.9Hz, 2H(P-C<u>H</u>$_2$)); 1.68(q, $^3J_{HH}$ 7.0Hz, $^3J_{HH}$ 8.0Hz, 2H(C<u>H</u>$_2$-CH_3)); 1.46(d, $^3J_{HH}$ 6.8Hz, 3H, CHC<u>H</u>3)); 0.91(t,$^3J_{HH}$ 8.0Hz, 3H, (CH_2-C<u>H</u>3)); ^{31}P NMR($CDCl_3$) δ/ppm: ^{31}P 17.1; pale yellow oil; Yield (%) 78

15. *Methyl N,N-diethyl-P-(3-methyl-2-oxopentyl)phosphonoamidate,* $C_{11}H_{24}NO_3P$; Calcd.: P 12.42, Found: P 12.30 %; IR: ν(cm^{-1}) 1700 $_{(C=C)}$, 1238 (P=O), 980 (P-O-C), ^{1}H NMR ($CDCl_3$): δ/ppm 3.39(d, $^3J_{HP}$ 10.09Hz, 3H, (OMe)); 3.09(t, $^2J_{HH}$ 5.8Hz, 1H(C<u>H</u>)); 2.50(d, $^2J_{HP}$ 11.9Hz, 2H(P-C<u>H</u>$_2$)); 2.93(m, $^3J_{HP}$ 13.6Hz, $^3J_{HH}$ 7.2Hz, 2H, (CH_3-C<u>H</u>$_2$-N)); 1.00 (t, $^3J_{HH}$ 7.2Hz, 3H, (C<u>H</u>$_3$-CH_2-N)); 1.68(q, $^3J_{HH}$ 7.0Hz, $^3J_{HH}$ 8.0Hz, 2H(C<u>H</u>$_2$-CH_3)); 1.40(d, $^3J_{HH}$ 6.8Hz, 3H, CHC<u>H</u>3)); 0.89(t,$^3J_{HH}$ 8.0Hz, 3H, (CH_2-C<u>H</u>3)); ^{31}P NMR(CDCl3) δ/ppm: ^{31}P 16.9; pale yellow oil; Yield (%) 84

16. 1-(dimethylphosphoryl)-3-methylpentan-2-one $C_8H_{17}O_2P$; Calcd.: P1 7.57, Found: P 17.49 %; IR: ν(cm^{-1}) 1708 $_{(C=C)}$, 1238 (P=O), 980 (P-O-C), ^{1}H NMR ($CDCl_3$): δ/ppm 3.09(t, $^2J_{HH}$ 5.8Hz, 1H(C<u>H</u>)); 2.50(d, $^2J_{HP}$ 11.9Hz, 2H(P-C<u>H</u>$_2$)); 1.76(d, $^2J_{HP}$ 16.6Hz, 6H(C<u>H</u>$_3$-P)); 1.68(q, $^3J_{HH}$ 7.0Hz, $^3J_{HH}$ 8.0Hz, 2H(C<u>H</u>$_2$-CH_3)); 1.40(d, $^3J_{HH}$ 6.8Hz, 3H, CHC<u>H</u>3)); 0.89(t,$^3J_{HH}$ 8.0Hz, 3H, (CH_2-C<u>H</u>3)); ^{31}P NMR($CDCl_3$) δ/ppm: ^{31}P 17.6; oil; Yield (%) 81.

17. *1-(diphenylphosphoryl)-3-methylpentan-2-one,* $C_{28}H_{21}O_2P$; Calcd.: P 7.37, Found: P 7.17 %; IR: ν(cm^{-1}) 1698 $_{(C=C)}$, 1238 (P=O), 980 (P-O-C), ^{1}H NMR ($CDCl_3$): δ/ppm 7.29-7.17(m, 2H, (Ph)); 7.05(d, 2JHH 7.75Hz, 1H, (Ph)); 6.89(t, 2JHH 7.25Hz, 2H, (Ph)); 3.09(t, $^2J_{HH}$ 5.8Hz, 1H(C<u>H</u>)); 2.50(d, $^2J_{HP}$ 11.9Hz, 2H(P-C<u>H</u>$_2$)); 1.68(q, $^3J_{HH}$ 7.0Hz, $^3J_{HH}$ 8.0Hz, 2H(C<u>H</u>$_2$-CH_3)); 1.40(d, $^3J_{HH}$ 6.8Hz, 3H, CHC<u>H</u>3)); 0.89(t,$^3J_{HH}$ 8.0Hz, 3H, (CH_2-C<u>H</u>3)); ^{31}P NMR(CDCl3) δ/ppm: ^{31}P 17.0; oil; Yield (%) 85.

Conclusions

The results obtained by us confirm once again the general mechanism of the reaction of nucleophilic addition of alcohols to 1,2-alkadienephosphonates, i.e. with formation of 1,2- and 2,3-adducts.

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