Alkyl alkynylphosphonites in the Kabachnik—Fields reaction*

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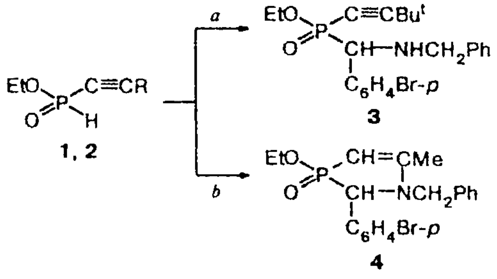
O-Ethyl alkynylphosphonites [EtOP(O)(H)C≡CR] (**1** and **2**) react with *p*-bromobenzaldehyde and benzylamine to form the usual acyclic products of the Kabachnik—Fields reaction or phosphorus-containing heterocycles depending on the nature of the substituent R at the β-carbon atom of the acetylene fragment of phosphonite. In the case of R = Bu^t, *O*-ethyl (α-benzylamino-*p*-bromobenzyl)(3,3-dimethylbut-1-ynyl)phosphinate (**3**) was obtained. In the case of R = Me, 1-benzyl-2-*p*-bromophenyl-3-ethoxy-5-methyl-3-oxo-Δ^4-1,3-λ^5-azaphospholine (**4**) was formed. Compounds **3** and **4** were also synthesized by the reactions of the above-mentioned phosphonites with the corresponding azomethines.

Key words: *O*-alkyl alkynylphosphonites, Kabachnik—Fields reaction; *O*-ethyl (α-benzylamino-*p*-bromobenzyl)(3,3-dimethylbut-1-ynyl)phospinate, 1-benzyl-2-*p*-bromophenyl-3-ethoxy-5-methyl-3-oxo-Δ^4-1,3-λ^5-azaphospholine, synthesis, IR and NMR spectra.

The Kabachnik—Fields reaction[1] is the major method for the synthesis of α-aminoalkyl derivatives of four-coordinate phosphorus acids. These acids are of great interest as physiologically active compounds. It is known[2] that the reactions of hydrophosphoryl compounds with amines and carbonyl compounds (the Kabachnik—Fields reaction) usually afford products identical to those obtained in the reactions with azomethines, which were prepared from the same amines and carbonyl compounds. Recently, we have demonstrated[3] that the reaction of *N*-benzylidenemethylamine with *O*-methyl 2-phenylethynylphosphonite (the hydrophosphoryl compound containing the α,β-acetylene group at the phosphorus atom) gave the five-membered heterocycle, namely, substituted Δ^4-1,3-azaphospholine. It was of interest to study the possibility of the synthesis of such heterocycles by the Kabachnik—Fields reaction. This reaction has not been studied previously for α,β-unsaturated compounds.

We found that the reactions of *O*-ethyl alkynylphosphonites (**1** and **2**) with benzylamine and *p*-bromobenzaldehyde afforded acyclic α,β-acetylene phosphinate (**3**) or substituted Δ^4-1,3-azaphospholine (**4**) depending on the structure of the substituent at the β-C atom of the acetylene group in the initial phosphonites **1** and **2**. Thus, the reaction of *O*-ethyl 3,3-dimethylbut-1-ynylphosphonite (**1**) gave *O*-ethyl (α-benzylamino-*p*-bromobenzyl)(3,3-dimethylbut-1-ynyl)phosphinate (**3**), while the reaction of *O*-ethyl prop-1-ynylphosphonite (**2**) afforded 1-benzyl-2-*p*-bromophenyl-3-ethoxy-5-methyl-3-oxo-Δ^4-1,3-azaphospholine (**4**) (Scheme 1).

Scheme 1



R = Bu^t (**1**), Me (**2**)

Reagents: *a*. $p\text{-BrC}_6\text{H}_4\text{C(O)H} + \text{PhCH}_2\text{NH}_2$;
b. $p\text{-BrC}_6\text{H}_4\text{CH=NCH}_2\text{Ph}$.

Apparently, the reaction proceeds through *N*-*p*-bromobenzylidenebenzylamine as an intermediate followed by addition of α,β-acetylene hydrophosphoryl compound **1** or **2** at the C=N bond of azomethine. If the β-C atom of the C≡C bond has a small electron-withdrawing substituent (for example, the methyl group), which favors β-addition, the resulting α-aminobenzyl phosphinate **3** (or its deprotonated *N*-anionic form) enters into the reaction of intramolecular addition at the C≡C bond. If the β-C atom of the C≡C bond carries a group that causes steric hindrances to nucleophilic addition (for example, the *tert*-butyl group) cyclization does not occur. The reactions of phosphonites **1** and **2** with *N*-*p*-bromobenzylidenebenzylamine (method (*b*)), which has been prepared previously from *p*-bromobenzaldehyde and benzylamine, gave analogous results. The yields of compounds **3** and **4** synthesized according to this proce-

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dure and those obtained by the Kabachnik—Fields reaction (method (*a*)) differ only slightly. Taking into account that the Kabachnik—Fields reaction is a one-step procedure for the preparation of phosphonate **3** and azaphospholine **4**, this reaction should be preferred for the synthesis of the above-mentioned compounds.

Phosphinate **3** and azaphospholine **4** are yellowish crystalline compounds, which are readily soluble in DMSO and acetone, soluble in chloroform and benzene, and poorly soluble in hexane. The ^{31}P NMR spectrum of phosphinate **3** has a signal with the δP chemical shift of 15.8 typical of acetylene phosphinates. The ^{31}P NMR spectrum of azaphospholine **4** has a signal with the δP chemical shift of 55.7 typical of 1,3-azaphospholines and 1,3-oxaphospholenes. The IR spectrum of phosphinate **3** shows an absorption band of the C≡C bond of the 3,3-dimethylbut-1-ynyl substituent (as a doublet at 2220 and 2180 cm^{-1}) and an absorption band of the NH group (3375 cm^{-1}). These bands are absent in the IR spectrum of phospholine **4**. The structure of heterocycle **4** was confirmed by the presence of a doublet of the alkenyl proton (δ 4.71) with the spin-spin coupling constant $^2J_{PH}$ = 17.1 Hz in the ^1H NMR spectrum. The methylene protons of the NCH_2 group in compounds **3** and **4** are anisochronous and show up as pairs of doublets with the spin-spin coupling constants $^2J_{H-H}$ of 13.7 and 16.5 Hz, respectively.

Therefore, we show the new possibilities of the Kabachnik—Fields reaction in the synthesis of organophosphorus compounds by preparing heterocycle **4** by the reaction of monoethyl 1-propynylphosphonite with *p*-bromobenzaldehyde and benzylamine.

Experimental

The IR spectra of compounds **3** and **4** were recorded on an IKS-29 instrument as KBr pellets. The ^1H NMR spectra were obtained on a Bruker AC-200 instrument (200.13 MHz). The ^{31}P NMR spectra were measured on a Bruker AC-200 instrument operating at 16.2 MHz; the chemical shifts were measured relative to a 85% H_3PO_4 solution.

***O*-Ethyl (α-benzylamino-*p*-bromobenzyl)(3,3-dimethylbut-1-ynyl)phosphinate (3).** *A. According to the Kabachnik—Fields reaction.* Benzylamine (0.01 mol) and *p*-bromobenzaldehyde (0.01 mol) were successively added to a solution of *O*-ethyl 3,3-dimethyl-1-butynylphosphonite **1** (0.01 mol) in benzene (5 mL). The reaction mixture was refluxed for 3 h and cooled to 20 °C. Then hexane (5 mL) was added. The product that precipitated was filtered off. Phosphinate **3** was obtained in 74% yield, m.p. 113—115 °C (from a 1 : 1 acetone—hexane mixture). Found (%): C, 60.17; H, 6.05; P, 6.80. $C_{22}H_{27}BrNO_2P$. Calculated (%): C, 58.94; H, 6.07; P, 6.91. IR, ν/cm^{-1}: 3375 (NH); 2220, 2180 (C≡C); 1238 (P=O); 1047 (POC). ^1H NMR ($CDCl_3$), δ: 1.18 (s, 9 H, Bu^t); 1.30 (t, 3 H, $C\underline{H}_3CH_2O$); 2.30 (br.s, 1 H, NH); 3.57 and 3.86 (both d, both 1 H, CH_2N, $^2J_{H-H}$ = 13.7 Hz); 3.98 (d, 1 H, PCHN, $^2J_{P-H}$ = 17.0 Hz); 4.08 (m, 2 H, CH_2O); 7.18—7.54 (m, 9 H, C_6H_5 + *n*-BrC_6H_4). ^{31}P NMR ($CHCl_3$), δ: 15.8.

B. From N-p-bromobenzylidenebenzylamine. A solution of *N*-*p*-bromobenzylidenebenzylamine (0.01 mol) in benzene (5 mL) was added to a solution of phosphonite **1** (0.01 mol) in benzene (5 mL). The reaction mixture was refluxed for 3 h. Then the solution was evaporated to half its initial volume under reduced pressure. Hexane (5 mL) was added, and the product that precipitated was filtered off. Compound **3** was obtained in 78% yield, m.p. 113—115 °C (from a 1 : 1 acetone—hexane mixture). The spectral characteristics are identical to those of the sample prepared according to method *A*.

1-Benzyl-2-*p*-bromophenyl-3-ethoxy-5-methyl-3-oxo-Δ^4-1,3-λ^5-azaphospholine (4) was prepared as described above both by the Kabachnik—Fields reaction (method *A*) and starting from *N*-*p*-bromobenzylidenebenzylamine (method *B*) using *O*-ethyl prop-1-ynylphosphonite **2** as the hydrophosphoryl compound. The yield was 64% (method *A*) and 70% (method *B*), m.p. 150—151 °C (from a 1 : 1 benzene—hexane mixture). Found (%): C, 55.98; H, 5.24; P, 7.87. $C_{19}H_{21}BrNO_2P$. Calculated (%): C, 56.17; H, 5.21; P, 7.62. IR, ν/cm^{-1}: 1550 (C=C); 1220 (P=O); 1022 (POC). ^1H NMR (DMSO-d_6), δ: 0.75 (t, 3 H, $C\underline{H}_3CH_2O$); 2.13 (s, 3 H, CH_3C=); 3.06 (m, 1 H, CH_2O); 3.51 (m, 1 H, CH_2O); 3.83 and 4.19 (both d, both 1 H, CH_2N, $^2J_{H-H}$ = 16.5 Hz); 4.51 (d, 1 H, PCHN, $^2J_{P-H}$ = 15.5 Hz); 4.71 (d, 1 H, PCH=, $^2J_{P-H}$ = 17.1 Hz); 6.97—7.64 (m, 9 H, C_6H_5 + *n*-BrC_6H_4). ^{31}P NMR ($CHCl_3$), δ: 55.7.

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