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Features of the Reaction of 4-Bromobut-2-enylphosphonium Salts with Monosubstituted Hydrazines

M. Zh. Ovakimyan, G. Ts. Gasparyan, M. R. Grigoryan, and A. S. Bichakhchyan

Scientific and Technological Center of Organic and Pharmaceutical Chemistry,
Institute of Organic Chemistry, National Academy of Sciences of the Republic of Armenia,
pr. Azatutyan 26, Yerevan, 0014 Armenia
e-mail: meri-grigoryan19@rambler.ru

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Abstract—(4-Bromobut-2-en-1-yl)triphenylphosphonium bromide reacted with phenylhydrazine at 2°C in the presence of sodium carbonate to form triphenyl[4-(2-phenylhydrazinylidene)but-2-en-1-yl]phosphonium bromide in 62% yield. The obtained *N*-phenylhydrazine derivatives cyclized into the corresponding pyrazoline derivatives of phosphonium salts. Unlike phenylhydrazine, ethylhydrazine reacted with (4-bromobut-2-ene-1-yl)triphenylphosphonium bromide under the same conditions to afford triphenyl[(1-ethyl-4,5-dihydro-1*H*-pyrazol-3-yl)methyl]- and -[(1-ethyl-1*H*-pyrazol-3-yl)methyl]phosphonium bromides in yields of 60 and 40%.

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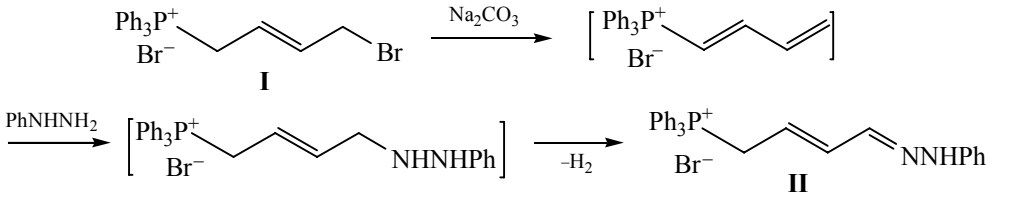
It is known that α,β- and β,γ-unsaturated phosphonium salts as well as their 1,3-diene analogs are convenient substrates for the preparation of β- and δ-substituted phosphonium salts. The latter are both of theoretical and practical interest due to their possible use in various fields of national economy and medicine [1–6].

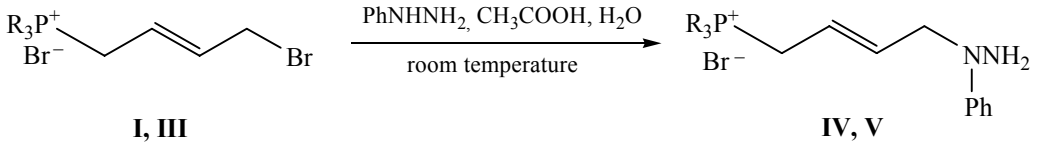
Previously we have showed that triphenyl- and tributylphosphonium salts containing potential buta-1,3-diene or 3-chlorobuta-1,3-diene fragments reacted with a three-fold molar amount of phenylhydrazine under heating in chloroform to form the 1,4-adducts. The latter undergo dehydrogenation to afford the corresponding hydrazone derivatives [7, 8].

In the continuation of these studies we performed the reaction of (4-bromobut-2-enyl)triphenylphosphonium bromide **I** with phenylhydrazine in chloroform at 2°C using sodium carbonate as a base. Triphenyl[4-(2-phenylhydrazinylidene)but-2-en-1-yl]-phosphonium bromide **II** was obtained in a 62% yield.



I **II**

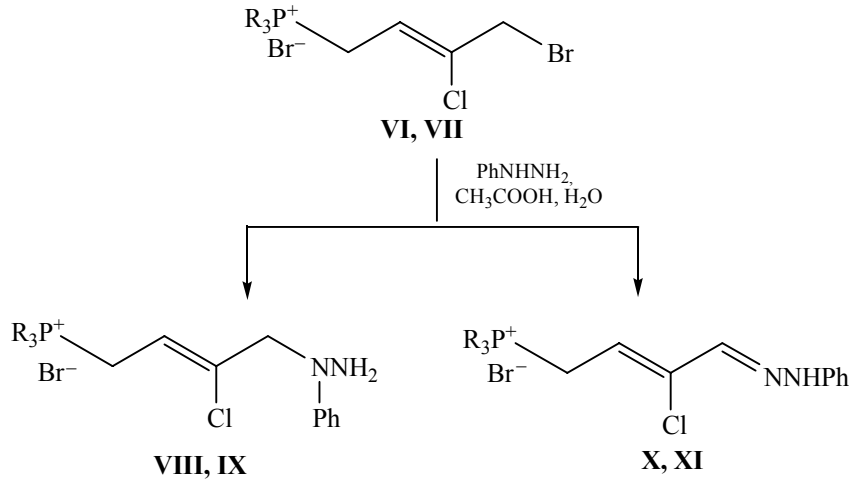
In order to suppress the 1,4-cleavage we carried out reactions of salt **I** and its tributyl analog **III** with a two-fold molar amount of phenylhydrazine in the presence of aqueous acetic acid at room temperature. The reactions proceeded exclusively as nucleophilic substitution involving the substituted nitrogen atom of phenylhydrazine to give the desired products **IV** and **V** in high yields.



I, III **IV, V**

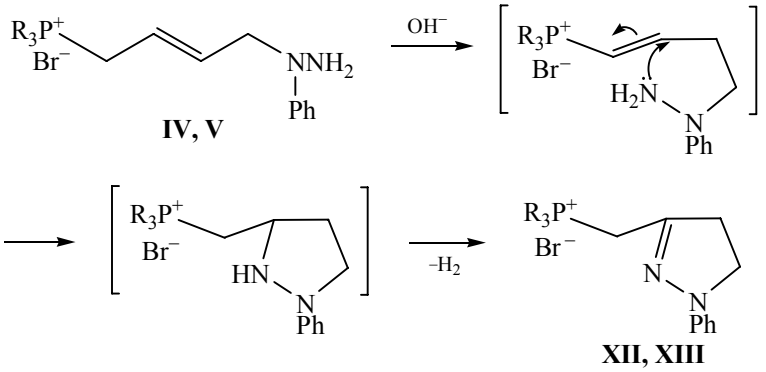
I, IV: R = Ph; **III, V**: R = C_4H_9.

However, we failed to obtain only the products of nucleophilic substitution under the same conditions proceeding from triphenyl- and tributyl(4-bromo-3-chlorobut-2-en-1-yl)phosphonium bromides **VI** and **VII**. In both cases compounds **X** and **XI** were obtained along with the substitution products **VIII** and **IX**.



VI, VIII, **X**: R = Ph; **VII, IX, XI**: R = Bu.

Compounds **IV** and **V** readily undergo heterocyclization. Their interaction with 25% aqueous solution of sodium hydroxide in benzene even at room temperature afforded the corresponding pyrazolines **XII** and **XIII** in >50% yield. Apparently, the reaction proceeds according to the following scheme.



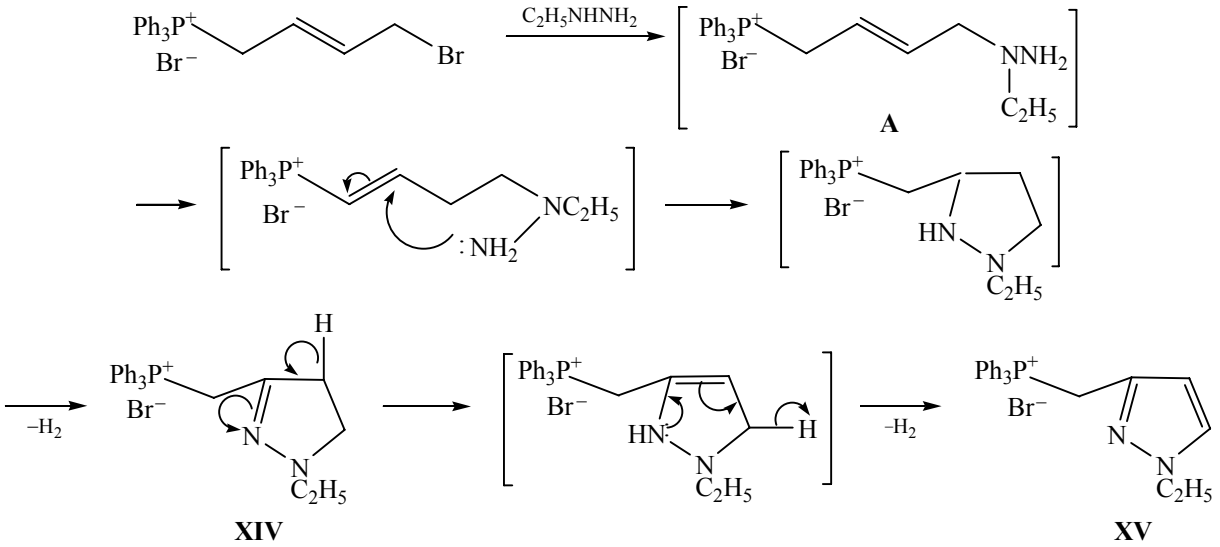
IV, XII: R = Ph; **V, XIII**: R = Bu.

α,β-Unsaturated intermediates formed from **IV** and **V** as a result of the prototropic isomerization undergo heterocyclization into *N*-phenylpyrazolidine derivatives. Under the reaction conditions the latter were subjected to spontaneous dehydrogenation [4, 5] resulting in the corresponding pyrazolines **XII** and **XIII**. Compounds **XII** and **XIII** have been previously prepared by reacting phenylhydrazine with triphenyl- and tributyl-(4-bromobut-2-yn-1-yl)phosphonium bromide [9].

Unlike phenylhydrazine, ethylhydrazine reacted with salt **I** to form pyrazoline **XIV** and pyrazole **XV** derivatives in acetonitrile at 30–35°C in the absence of a base. Probably, the reaction proceeds via the intermediate formation of the substitution product **A** of linear structure subjected to heterocyclization under the reaction conditions (Scheme 1).

Different behavior of phenyl- and ethylhydrazine may be due to the difference between their nucleophilicity. Probably, the formation of compound **XV** is due to the release of a hydride ion owing to the transfer of a lone electron pair on the nitrogen in the dihydropyrazole molecule by the above mentioned scheme, which is in agreement with the literature data on hydride-donor properties of dihydroaromatic compounds [10].

Scheme 1.



EXPERIMENTAL

^{1}H (300.077 MHz) and ^{31}P (121.47 MHz) NMR spectra were recorded on a Varian Mercury-300 spectrometer at 303 K using a mixture DMSO-d_6–CCl_4 (1 : 3) as a solvent. Chemical shifts are shown relative to internal refernce TMS (^{1}H) and external reference 85% H_3PO_4 (^{31}P), respectively.

Triphenyl- and tributyl(4-bromobut-2-en-1-yl)phosphonium bromides **I** and **III**, triphenyl- and tributyl(4-bromo-3-chlorobut-2-en-1-yl)phosphonium bromides **VI** and **VII** were synthesized according to known methods [11, 12].

Triphenyl[4-(2-phenylhydrazinylidene)but-2-en-1-yl]phosphonium bromide (II). A mixture of 1.5 g (3.2 mmol) of salt **I** and 1.32 g (9.6 mmol) of powdered sodium carbonate in 20 mL of chloroform was stirred for 18 h at room temperature. The reaction mixture was filtered. Then 0.38 g (3.5 mmol) of phenylhydrazine was added dropwise to the filtrate at 2°C. After heating to room temperature, water was added to the reaction mixture. The organic layer was separated, dried over $MgSO_4$ and evaporated. The residue was recrystallized from ethyl acetate–isopropyl alcohol mixture. Yield 1 g (62%), mp 218–220°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.8 d.d (2H, P^+CH_2, J_1 16.10, J_2 7.95), 5.48–5.87 m (1H, $P^+CH_2CH{=}C\underline{H}$), 6.37–6.49 m (1H, $P^+CH_2C\underline{H}{=}CH$), 6.64 t.t (1H, H^4_{Ph}, J_1 7.30, J_2 1.30), 6.98 d.d (2H, $H^{3,5}_{Ph}$, J_1 8.41, J_2 7.33), 7.10 d.d (2H, $H^{2,6}_{Ph}$, J_1 8.41, J_2 1.30), 7.48 d (1H, CH=N, *J* 7.3), 7.6–8.0 m (15H, P^+Ph), 10.25 s (1H, NNH). ^{31}P NMR spectrum: δ_P 26.28 ppm. Found, %: Br 15.73; P 5.87. $C_{28}H_{26}BrN_2P$. Calculated, %: Br 15.97; P 6.19.

Triphenyl[4-(1-phenylhydrazinyl)but-2-en-1-yl]-phosphonium bromide (IV). A mixture of 0.12 mL of acetic acid and 0.45 g (4.2 mmol) of phenylhydrazine was added to a suspension of 1 g (2.1 mmol) of salt **I** in 15 mL of water at room temperature. The reaction mixture was stirred for 4 h. Then the reaction product was extracted with chloroform. The organic layer was separated, dried over $MgSO_4$, filtered, and evaporated. The residue was thoroughly washed with benzene and anhydrous diethyl ether, and dried in a vacuum. Yield 0.75 g (71%), mp 98–101°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.95 br.s (2H, NH_2), 3.9–4.1 m (2H, CH_2NPh, J_1 7.35, J_2 1.50), 4.63 d.d (2H, P^+CH_2, J_1 16.12, J_2 7.95), 5.45–5.55 m (1H, $P^+CH_2CH{=}C\underline{H}$), 5.83–6.01 m (1H, $P^+CH_2C\underline{H}{=}CH$), 6.6–7.0 m (5H, NPh), 7.6–7.92 m (15H, P^+Ph). ^{31}P NMR spectrum: δ_P 26.8 ppm. Found, %: Br 15.67; P 5.79. $C_{28}H_{28}BrN_2P$. Calculated, %: Br 15.90; P 6.16.

Tributyl[4-(1-phenylhydrazinyl)but-2-en-1-yl]-phosphonium bromide (V) was obtained similarly from 1 g (2.4 mmol) of the salt **III** and 0.5 g (4.8 mmol) of phenylhydrazine in the presence of 0.14 mL of acetic acid in 15 mL of water. Yield 0.9 g (84.7%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 br.t (9H, $3CH_3$, *J* 6.70), 1.4–1.5 m (12H, $3CH_2$), 2.11–2.29 m (6H, $3CH_2$), 2.95 br.s (2H, NH_2), 3.24 d.d (2H, P^+CH_2, J_1 16.30, J_2 8.00), 4.19 d.d (2H, CH_2NPh, J_1 7.30, J_2 1.50), 5.58–5.72 m (1H, $P^+CH_2CH{=}C\underline{H}$), 5.85–

6.07 m (1H, $P^+CH_2C\underline{H}$=CH), 6.8 t.t (1H, H^4_{Ph}, J_1 7.30, J_2 1.30), 6.98–7.1 m (2H, $H^{3,5}_{Ph}$), 7.15–7.25 m (2H, $H^{2,6}_{Ph}$). ^{31}P NMR spectrum: δ_P 37.75 ppm. Found, %: Br 17.85; P 6.74. $C_{22}H_{40}BrN_2P$. Calculated, %: Br 18.06; P 6.99.

Triphenyl[4-(1-phenylhydrazinyl)-3-chlorobut-2-en-1-yl]phosphonium bromide (VIII) was obtained similarly from 2.5 g (4.9 mmol) of the salt **VI** and 1.1 g (9.8 mmol) of phenylhydrazine in the presence of 0.28 mL of acetic acid in 20 mL of water. The product was isolated by fractional recrystallization from ethyl acetate–2-propanol mixture. Yield 1.5 g (56.8%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.98 br.s (2H, NH_2), 3.58 д (2H, $C\underline{H}_2$NPh, *J* 1.30), 4.87 d.d (2H, P^+CH_2, J_1 16.30, J_2 8.00), 5.96–6.12 m (1H, $P^+CH_2C\underline{H}$=CCl), 6.66 t.t (1H, H^4_{Ph}, J_1 7.30, J_2 1.30), 6.98–7.08 m (2H, $H^{3,5}_{Ph}$), 7.14–7.22 m (2H, $H^{2,6}_{Ph}$), 7.65–8.0 m (15H, P^+Ph). ^{31}P NMR spectrum: δ_P 26.2 ppm. In addition triphenyl[4-(2-phenylhydrazinylidene)-3-chlorobut-2-en-1-yl]phosphonium bromide **X** was obtained (0.6 g, 2 2.9%). ^{1}H and ^{31}P NMR spectra coincided with those of the known sample [7]. Found,%: Br 14.43; P 6.04. $C_{28}H_{27}BrClN_2P$. Calculated, %: Br 14.86; P 5.76.

Tributyl[4-(1-phenylhydrazinyl)-3-chlorobut-2-en-1-yl]phosphonium bromide (IX) was obtained similarly from 1.5 g (3.3 mmol) of the salt **VII** and 0.8 g (7.0 mmol) of phenylhydrazine in the presence of 0.19 mL of acetic acid in 15 mL of water. The product was isolated by fractional recrystallization from ethyl acetate–2-propanol mixture. Yield 0.8 g (50%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 br.t (9H, $3CH_3$, *J* 6.70), 1.32–1.58 m (12H, $3CH_2$), 2.38–2.47 m (6H, $3CH_2$), 3.05 br.s (2H, NH_2), 3.42 d.d (2H, P^+CH_2, J_1 16.40, J_2 7.10), 4.21 d (2H, $C\underline{H}_2$NPh, J_1 1.60), 5.82–6.08 m (1H, $^+CH_2CH$=CCl), 6.7 t.t (1H, H^4_{Ph}, J_1 7.30, J_2 1.30), 6.94–7.04 m (2H, $H^{3,5}_{Ph}$), 7.11–7.25 m (2H, $H^{2,6}_{Ph}$). ^{31}P NMR spectrum: δ_P 40.36 ppm.

In addition tributyl[4-(2-phenylhydrazinylidene)-3-chlorobut-2-en-1-yl]phosphonium bromide **XI** was obtained (0.4 g, 25 %). ^{1}H and ^{31}P NMR spectra coincided with those of the known sample [7]. Found, %: Br 16.43; P 6.07. $C_{22}H_{39}BrClN_2P$. Calculated, %: Br 16.75; P 6.49.

Triphenyl[(1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)methyl]phosphonium bromide (XII). A mixture of 1.5 g (3.0 mmol) of salt **IV** and 1 g (6.2 mmol) of 25% aqueous solution of sodium hydroxide in 20 mL of benzene was stirred for 3 h at room temperature. The benzene layer was separated. Then water and chloroform were added to the residue. Triphenylphosphine oxide (mp 156°C) was isolated from the benzene layer (0.2 g, 24%). The chloroform extract was dried over $MgSO_4$, filtered and evaporated. The residue was washed with anhydrous diethyl ether, dried in a vacuum, and recrystallized from ethyl acetate–2-propanol mixture. Yield 0.8 g (53%). ^{1}H and ^{31}P NMR spectra coincided with those of the known sample [9].

Tributyl[(1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-methyl]phosphonium bromide (XIII) was prepared similarly from 1.5 g (3.4 mmol) of salt **V** and 1.1 g (6.8 mmol) of 25% aqueous sodium hydroxide in 20 mL of benzene. Yield 0.76 g (51%). ^{1}H and ^{31}P NMR spectra coincided with those of the known sample [9].

Triphenyl[(1-ethyl-4,5-dihydro-1*H*-pyrazol-3-yl)-methyl]phosphonium bromide (XIV) and triphenyl [(1-ethyl-1*H*-pyrazol-3-yl)methyl]phosphonium bromide (XV). A mixture of 1 g (2.1 mmol) of salt **I** and 0.25 g (4.2 mmol) of ethylhydrazine in 15 mL of acetonitrile was stirred at 30–35°C for 8 h. Then the solvent was removed, and the reaction products were extracted from the residue with water and chloroform. The chloroform layer was dried over $MgSO_4$, filtered and evaporated. The residue was washed with benzene and anhydrous diethyl ether, and dried in a vacuum. Yield 0.8 g (**XIV**:**XV** = 3:2).

Compound XIV. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.24 t (3H, $CH_2C\underline{H}_3$, *J* 7.3), 2.73 t. d (2H, CH_2, J_1 10.3, J_2 1.8), 3.40 q (2H, $C\underline{H}_2CH_3$, *J* 7.3), 3.65 t (2H, NCH_2, *J* 10.3), 5.2 d (2H, P^+CH_2, *J* 15.1), 7.62–7.8 m (15H, P^+Ph_3). ^{31}P NMR spectrum: δ_P 27.3 ppm.

Compound XV. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.12 t (3H, $CH_2C\underline{H}_3$, *J* 7.3), 4.05 q (2H, $C\underline{H}_2CH_3$), 5.09 d (2H, P^+CH_2, *J* 15.1), 5.87 d.d (1H, H^4_{Pyr}, J_1 2.4, J_2 1.5), 7.45 d (1H, H^5_{Pyr}, *J* 2.4), 7.82–8.0 m (15H, P^+Ph_3). ^{31}P NMR spectrum: δ_P 27.5 ppm.

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