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Reactions of Phosphonioalkyl Derivatives of Phenylhydrazine and Hydroxylamine

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Abstract — Triphenyl- and tributyl[2-(2-phenylhydrazino)ethyl]phosphonium salts undergo dehydrogenation on heating to form the corresponding phenylhydrazones in high yields. The phenylhydrazone formed from the triphenylphosphonium salt can also be prepared from triphenyl(1-alkoxy-2-bromoethyl)phosphonium bromides. The latter reaction is proposed to involve reduction of the COC group with phenylhydrazine. *N*,*N*-Diphosphonioethylation and *N*,*N*-diphosphoniopropylation of hydroxylamine are performed. Alkaline hydrolysis of the resulting diphosphonium salts gave *N*,*N*-bis[2-(diphenylphosphoryl)ethyl(propyl)]hydroxylamines in high yields.

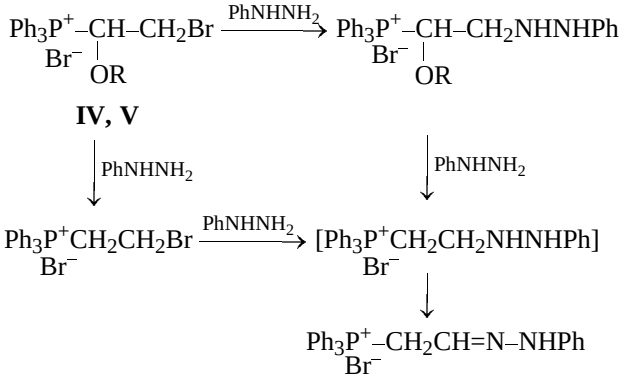
Previously we found that triphenyl[2-(2-phenylhydrazino]ethyl]phosphonium bromide (**I**) reacts with aqueous sodium hydroxide to form *cis*- and *trans*-(diphenylphosphoryl)acetaldehyde phenylhydrazone [1].

Further studies showed that the phenylhydrazone is also formed from salt **I** in the absence of alkali. Thus, refluxing of salt **I** in ethanol or DMF at 100°C for some hours gave a mixture of *cis*- and *trans*-triphenyl[2-(phenylhydrazono)ethyl]phosphonium bromides in high yield.

$$\underset{\mathbf{I}}{Ph_3P^+CH_2CH_2NHNHPh\ Br^-} \longrightarrow \underset{\mathbf{II}}{Ph_3P^+CH_2CH{=}NNHPh\ Br^-}.$$

Phosphoniophenylhydrazone **II** is also formed by alkylation of salt **I** with propargyl bromide and of the tributylphosphonium analog of salt **I** (compound **III**) with acrylonitrile in methanol under reflux. Note that the reaction of (4-bromo-3-chlorobut-2-enyl)triphenylphosphonium bromide with phenylhydrazine was performed in a similar way [2]. This reaction is likely to involve deprotonation of the hydrazine nitrogen atom followed by expulsion of the neighboring hydrogen atom that is almost as mobile as hydride hydrogen. Deprotonation, in its turn, is favored by the presence both of halide anions and of the lone electron pair of hydrazine nitrogen.

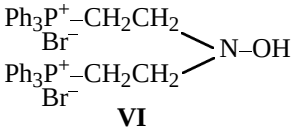
It is interesting to note that the reactions with phenylhydrazine with triphenylphosphonium salts with a 1-ethoxy- or 1-butoxy-2-bromoethyl group both gave, instead of expected nucleophilic substitution products, phosphoniophenylhydrazone **II** identical to that obtained from salt **I**, as well as much 1-alkoxyvinylphosphonium salts. Salt **II** is probably formed by a scheme involving reduction of the C–O–C bond with phenylhydrazine either directly in salts **IV** or **V** or after replacement of bromine with the phenyl=hydrazono group.



R = C_2H_5 (**IV**), C_4H_9 (**V**).

Previously we showed [1] that the reaction of ethylenebis(triphenylphosphonium) dibromide with equimolar amount of hydroxylamine in the presence of triethylamine affords [2-(hydroxylamino)ethyl)triphenylphosphonium bromide.

X-ray diffraction analysis established that compound **VI** is formed by dialkylation of hydroxylamine and has the following structure.



VI

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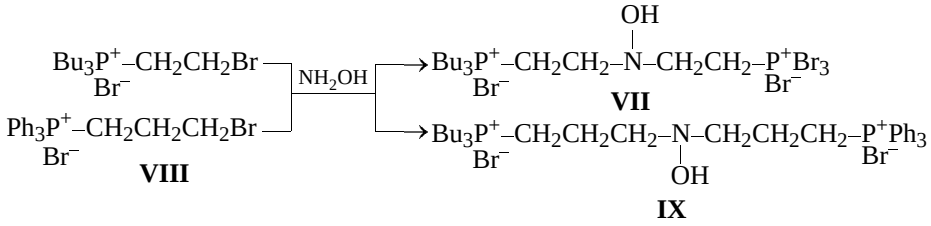
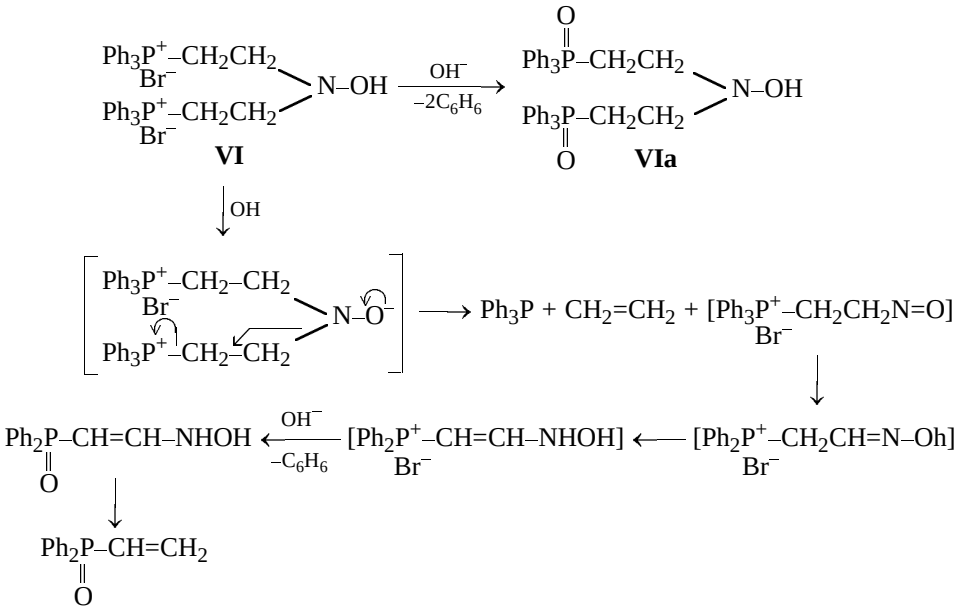
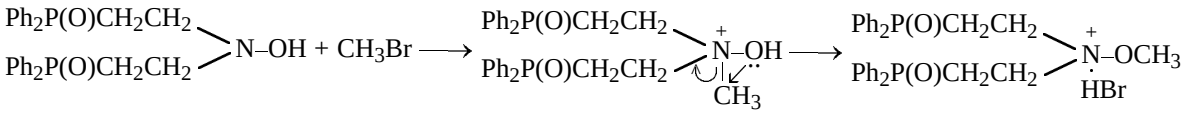
Attempted monoalkylation of the starting reagents failed. *N*,*N*-Dialkylation products were also prepared from (2-bromoethyl)tributylphosphonium and (3-bromopropyl)triphenylphosphonium bromides (**VIII**).



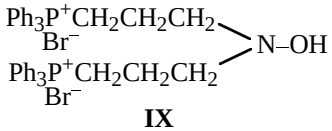
Hydrolysis of salt **VI** with aqueous alkali gave *N*,*N*-bis[2-(diphenylphosphoryl)ethyl]hydroxylamine along with small amounts of *cis*- and *trans*-(diphenylphosphoryl)hydroxylamines. On attempted recrystallization the latter converted into (diphenylphosphoryl)ethene according to the following scheme.



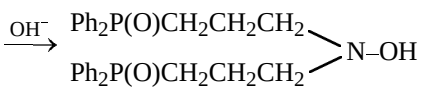
Dioxide **VIa** is readily alkylated with methyl bromide to form an *N*-methoxy derivative, whereas salt **VI** does not react under the same conditions. This fact is probably explained by electronic effects of the phosphonium groups, that operate to much reduce the nucleophilicity of the nitrogen atoms. The reaction probably occurs by the following scheme.



Hydrolysis of salt **IX** with aqueous alkali resulted in exclusive formation of dioxide **IXa**.



IX



IXa

EXPERIMENTAL

The ^{1}H, ^{31}P, and ^{13}C NMR spectra were obtained on a Varian Mercuri-300 instrument (300 MHz) in $CDCl_3$ and DMSO. Thin-layer chromatography was performed on Silufol UV-254 plates, developer iodine vapor. The starting salts were prepared by known procedures [1, 3].

Triphenyl[2-(phenylhydrazono)ethyl]phosphonium bromide. *a*. Triphenyl[2-(2-phenylhydrazino]-ethyl]phosphonium bromide (**I**), 0.5 g, was heated in 10 ml of DMF at 100°C for 9 h. The solvent was then distilled off, and the residue was washed with dry ether and dried in a vacuum to obtain 0.4 g (84%) of compound **II**, mp 190°C. ^{1}H NMR spectrum (DMSO), δ, ppm (*J*, Hz): 4.90 d.d (2H, *syn*-PCH_2, $^2J_{PH}$ 15.6, J_{HH} 5.0), 5.40 d.d (2H, *anti*-PCH_2, $^2J_{PH}$ 17.0, J_{HH} 5.7), 6.75–7.10 m (5H, NHC_6H_5), 7.60–8.00 m [16H, $P(C_6H_5)_3$, CH=N], 9.65 s and 10.20 s (1H, *syn*-, *anti*-NH). Found Br^-, %: 16.21. $C_{26}H_{24}BrN_2P$. Calculated Br^-, %: 16.84.

b. Propargyl bromide, 0.12 g, was added to a solution of 0.5 g of salt **I** in ethanol, and the mixture was refluxed for 5 h, after which the solvent was removed, and the residue was washed with dry ether to obtain 0.5 g of a substance whose recrystallization (isopropyl alcohol–benzene) gave 0.25 g (25%) of compound **II**. The melting point and ^{1}H NMR spectrum of the sample were consistent with those of the sample obtained by procedure *a*.

Tributyl[2-(2-phenylhydrazino)ethyl]phosphonium bromide (III). Phenylhydrazine, 3 g, was added to a solution of 5.5 g (2-bromoethyl)tributylphosphonium bromide in 25 ml of ethanol, and the reaction mixture was left to stand for 2 days. The solvent was then removed, and the residue was diluted with methylene chloride. Undissolved material was filtered off to obtain 2.6 g (98%) of phenylhydrazine hydrobromide (sublimed on melting above 195°C). The methylene chloride solution was evaporated, and the residue was washed with dry ether and dried to obtain 5.6 g of a solid material whose recrystallization (ethyl acetate–ethanol) gave 2.9 g (50%) of salt **III**, mp 95°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.91 t (9H, CH_3CH_2, J_{HH} 7.1), 1.56–1.35 m [12H, $CH_3(CH_2)_2CH_2$], 2.37–2.25 m [6H, $CH_3(CH_2)_2CH_2$], 2.79 d.t (2H, PCH2, J_{HH} 6.5, $^2J_{PH}$ 12.5), 3.34 d.t (2H, CH_2N, J_{HH} 6.5, $^3J_{PH}$ 17.1), 6.73 t (H, *p*-C_6H_5, J_{HH} 7.3), 6.92 d (2H, *o*-C_6H_5, J_{HH} 8.3), 7.13 d.d (2H, *m*-C_6H_5, J_{HH} 7.3, 8.5). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz): 18.60 d (PCH_2, J 42.2), 19.60 d [$PCH_2(CH_2)_2CH_3$, *J* 47.1], 13.46 [$PCH_2(CH_2)_2CH_3$], 23.87 [$PCH_2(CH_2)_2CH_3$], 44.24 (NCH_2), 149.06 (*ipso*-NC_6H_5), 129.02, 113.61 (*o*- and *m*-NC_6H_5), 119.17 (*p*-NC_6H_5). Found Br^-, %: 18.98. $C_{20}H_{38}BrN_2P$. Calculated Br^-, %: 19.18.

Tributyl[2-(phenylhydrazono)ethyl]phosphonium bromide. Acrylonitrile, 0.16 g, was added to a solution of 0.4 g of salt **III** in 10 ml of methanol, and the mixture was refluxed for 16 h. The solvent was then removed, and the residue was thoroughly washed with dry ether and recrystallized from ethyl acetate–ethanol to obtain 0.35 g (84%) of tributyl[2-(phenylhydrazono)ethyl]phosphonium bromide, mp 135°C, R_f 0.79 (isobutanol–acetic acid–water, 5 : 2 : 2). ^{1}H NMR spectrum (DMSO), δ, ppm (*J*, Hz): 1.00 t (9H, CH_3CH_2, J_{HH} 7.1), 1.35–1.56 m (12H, $CH_3CH_2CH_2 \cdot CH_2$), 2.25–2.37 m [6H, $CH_3(CH_2)_2CH_2$], 3.60 d.d (2H, *syn*-PCH_2, $^2J_{PH}$ 16.5, J_{HH} 5.0), 4.10 d.d (2H, *anti*-PCH_2, $^2J_{PH}$ 19.0, J_{HH} 5.7), 6.70 t (1H, *p*-C_6H_5, J_{HH} 7.3), 6.90 d (2H, *o*-C_6H_5, J_{HH} 8.3), 7.10 d.d (2H, *m*-C_6H_5, $1J_{HH}$ 7.3, $2J_{HH}$ 8.3), 7.30 m [1H, *syn*- and *anti*-CH=N], 10.20 s [1H, NNH].

Reaction of (2-bromo-1-ethoxyethyl)triphenylphosphonium bromide with phenylhydrazine. Phenylhydrazine, 0.8 g, was added to a solution of 1.8 g of salt **IV** in 20 ml of acetonitrile, and the mixture was left to stand at room temperature for 24 h. The solvent was then removed, and the residue was washed with dry ether and diluted with methylene chloride. Undissolved residue was filtered off and dried to obtain 0.65 g (94%) of phenylhydrazine hydrobromide (sublimed on melting above 195°C). The methylene chloride solution was evaporated to obtain 1.6 g of a mixture of phenylhydrazone **II** and (1-ethoxyvinyl)triphenylphosphonium bromide (1 : 4, ^{1}H NMR data). ^{1}H NMR spectrum of (1-ethoxyvinyl) triphenylphosphonium bromide ($CDCl_3$), δ, ppm (*J*, Hz): 1.40 t (3H, OCH_2CH_2, J_{HH} 6.5), 4.30 q (2H, OCH_2CH_3, J_{HH} 6.5), 5.10 d.d [1H, PC(O)CHH, $^2J_{PH}$ 129.0, J_{HH} 5.8], 6.00 d.d [1H, PC(O)CHH, $^3J_{PH}$ 41.0, J_{HH} 5.8], 7.60–7.80 m (15H, C_6H_5P). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 20.

Reaction of (2-bromo-1-butoxyethyl)triphenyl-

phosphonium bromide with phenylhydrazine. Phenylhydrazine, 0.7 g, was added to a solution of 1.8 g of salt **V** in 20 ml of acetonitrile, and the mixture was left to stand at room temperature for 24 h and then treated as described above to obtain 1.5 g of a mixture of (1-butoxyvinyl)triphenylphosphonium bromide and phenylhydrazone **II** (3:1, ^{1}H NMR data). ^{1}H NMR spectrum of (1-butoxyvinyl)triphenylphosphonium bromide ($CDCl_3$), δ, ppm (*J*, Hz): 0.90 t [3H, $O(CH_2)_3CH_3$, J_{HH} 6.5], 1.10–1.30 m [2H, $O(CH_2)_2 \cdot CH_2CH_3$], 1.60–1.80 m (2H, $OCH_2CH_2CH_2CH_3$), 4.10 t [2H, $OCH_2(CH_2)_2CH_3$, J_{HH} 6.5], 5.10 d.d [1H, PC(O)CHH, $^3J_{PH}$ 12.5, J_{HH} 6.0], 5.90 d.d [1H, PC(O)CHH, $^3J_{PH}$ 39.5, J_{HH} 6.0], 7.60–7.90 m [15H, $(C_6H_5)_3P$].

***N,N*-Bis[2-(tributylphosphonio)ethyl]hydroxylamine dibromide.** Triethylamine, 1.4 g, was added dropwise to a mixture of 5.4 g of (2-bromoethyl)tributylphosphonium bromide in 40 ml of methylene chloride and 0.5 g hydroxylamine hydrochloride. The mixture was left to stand for 3 days at room temperature and then diluted with water. The organic layer was separated and dried over magnesium sulfate. The solvent was removed, and the residue was dried and recrystallized (ethyl acetate–ethanol) to obtain 3.5 g (77%) of salt **VII**, mp 150°C. ^{1}H NMR spectrum (DMSO), δ, ppm (*J*, Hz): 1.00 m {18H, $P[(CH_2)_3 \cdot CH_3]_3$}, 1.50 m {24H, $P[CH_2(CH_2)_2CH_3]_3$}, 2.40 m {12H, $P[CH_2(CH_2)_2CH_3]_3$}, 2.65 d.t (4H, PCH_2, $^2J_{PH}$ 13.3, $^3J_{HH}$ 6.9), 3.33 d.t (4H, NCH_2, $^3J_{PH}$ 15.3, $^3J_{HH}$ 6.9). ^{31}P NMR spectrum (DMSO), δ_P, ppm: 38.84. Found Br^-, %: 24.30. $C_{28}H_{63}Br_2NOP_2$. Calculated Br^-, %: 24.58.

Alkaline hydrolysis of *N,N*-bis[2-(triphenylphosphonio)ethyl]hydroxylamine dibromide. To 3 g of salt **VI** {^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 3.33 d.t (4H, NCH_2, $^3J_{PH}$ 11.4, $^3J_{HH}$ 6.90), 3.78 d.t [4H, $(P^+CH_2)_2$, $^2J_{PH}$ 13.2, $^3J_{HH}$ 6.9], 7.62–7.86 m [30H, $P(C_6H_5)_3$], 8.75 s (1H, NOH)} in 15 ml of benzene, 1.2 ml of 25% aqueous solution of 0.6 g of sodium hydroxide, and the reaction mixture was refluxed for 12 h. The organic layer was separated, and the aqueous solution was treated with benzene. The combined benzene extracts were dried over magnesium sulfate and evaporated to leave 1.3 g of a mixture of triphenylphosphine oxide, *N,N*-bis[2-(diphenylphosphory)lethyl]hydroxylamine, and diphenyl-[2-(hydroxylamino)vinyl]phosphine oxide (^{1}H NMR data). Fractional crystallization of the mixture allowed the first two components to be separated pure and identified by the ^{1}H and ^{31}P NMR spectra. ^{31}P NMR spectrum of triphenylphosphine oxide, δ_P, ppm: 29.6. ^{1}H NMR spectrum of *N,N*-bis[2-(diphenylphosphoryl)-ethyl]hydroxylamine ($CDCl_3$), δ, ppm (*J*, Hz): 2.50 d.t (4H, PCH_2, $^2J_{PH}$ 12.9, J_{HH} 7.9), 2.90 d.t (4H, NCH_2, $^3J_{PH}$ 10.0, J_{HH} 7.9), 7.40–7.80 m [20H, $P(C_6H_5)_2$]. Repeated recrystallization of the third component from ethanol gave diphenyl(vinyl)phosphine oxide. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 6.20–6.40 m (2H, $PCHCH_2$), 6.60–6.80 m (1H, $PCHCH_2$), 7.40–7.80 m (10H, PC_6H_5). ^{31}P NMR spectrum ($CDCl_3$), δP, ppm: 24.50. Compound **VIa** was reacted with methyl bromide to obtain *N,N*-bis[2-(diphenylphosphory)lethyl]-*O*-methylhydroxylamine bromohydrate. ^{1}H NMR spectrum (DMSO), δ, ppm (*J*, Hz): 3.10 d.t (4H, PCH_2, $^2J_{PH}$ 12.9, $^3J_{HH}$ 7.9), 3.50 s (3H, $NOCH_3$), 4.00 d.t (4H, NCH_2, $^3J_{PH}$ 11.2, $^3J_{HH}$ 7.9), 7.40–7.85 m [20H, $(C_6H_5)_2P$], 12.30 br.s (1H, NH). ^{31}P NMR spectrum (DMSO), δ_P, ppm: 34.13. Found Br^-, %: 13.10. $C_{29}H_{32}BrNO_3P_2$. Calculated Br^-, %: 13.69.

Reaction of (3-bromopropyl)triphenylphosphonium bromide with hydroxylamine. Triethylamine, 0.9 g, was added dropwise to a solution of 2 g of salt **VIII** prepared as described in [3] [^{1}H NMR spectrum (DMSO), δ, ppm (*J*, Hz): 2.10 m (2H, $CH_2CH_2CH_2$), 3.70 t (2H, CH_2Br), 3.95 d.t (2H, P^+CH_2, $^2J_{PH}$ 13.9, $^3J_{HH}$ 6.8)] and 0.3 g of hydroxylamine hydrochloride in 10 ml of chloroform, and the reaction mixture was refluxed for 19 h. After cooling, the solution was diluted with water, the organic layer was separated, dried over magnesium sulfate, the solvent was removed, and the residue was dried to obtain 1.5 g (78%) of *N,N*-bis[3(triphenylphosphonio)-propyl]hydroxylamine dibromide (**IX**), mp 253–255°C. ^{1}H NMR spectrum (DMSO), δ, ppm (*J*, Hz): 1.80 m [4H, $(CH_2CH_2CH_2)_2$], 2.90 t (4H, CH_2N), 4.10 d.t [4H, $(PCH_2)_2$, $^2J_{PH}$ 12.0, $^3J_{HH}$ 6.8], 7.62–8.10 m {30H, $[P(C_6H_5)_3]_2$}. ^{31}P NMR spectrum (DMSO), δ_P, ppm: 30.73. Found Br^-, %: 19.95. $C_{42}H_{43}Br_2NOP_2$. Calculated Br^-, %: 20.02.

Alkaline hydrolysis of *N,N*-bis[3-(triphenylphosphonio)propyl]hydroxylamine dibromide. To a solution of 2 g of salt **IX** in 10 ml of benzene, 0.8 ml of a 25% aqueous solution of 0.4 g of sodium hydroxide, and the reaction mixture was refluxed for 3 h. Benzene was removed from the reaction mixture by steam distillation, and the residue was washed with water and dried to obtain 1.2 g (92%) of *N,N*-bis[3-(triphenylphosphoryl)propyl]hydroxylamine, mp 209–210°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.02 m [4H, $(CH_2CH_2CH_2)_2$], 2.50 d.t [4H, $(PCH_2)_2$, $^2J_{PH}$ 11.3, J_{HH} 7.0], 2.98 t [4H, $(CH_2)_2N$], 7.40–7.80 m [20H, $(PC_6H_5)_2$]. ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz): 18.60 d (CH_2, J_{PC} 3.5), 26.84 d (PCH_2, $^1J_{PC}$ 71.9), 59.94 d (NCH_2, $^2J_{PC}$ 9.6), 128.87 d (*m*-C_6H_5P, J_{PC} 11.7), 130.98 d (*o*-C_6H_5P, J_{PC} 9.4),

131.98 d (*p*-C_6H_5P, J_{PC} 2.6), 132.76 d (*ipso*-C_6H_5P, J_{PC} 99.80).

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