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Synthesis of 2-(Alkylsulfanyl)propyltriphenylphosphonium Bromides and Their Alkaline Hydrolysis with Potassium *tert*-Butoxide

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Abstract—A series of 2-(alkylsulfanyl)propyltriphenylphosphonium salts was obtained starting from allyltriphenylphosphonium bromide. Alkaline hydrolysis of the obtained sulfur-containing quaternary phosphonium salts by the action of potassium *tert*-butoxide afforded 2-(alkylsulfanyl)propyldiphenylphosphine oxides in high yields.

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Study of nucleophilic addition to quaternary phosphonium salts with both existing and potential vinyl groups are of great interest [1–4]. In this connection, allyltriphenylphosphonium bromide attracts particular attention. Ammonia, primary and secondary amines react readily with allyltriphenylphosphonium iodide to form *N*-substituted (2-aminopropyl)triphenylphosphonium salts [5].

In this work we synthesized a series of 2-(alkylsulfanyl)propyltriphenylphosphonium salts by sequential reacting equimolar amounts of allyltriphenylphosphonium bromide **I** with triethylamine and thiols.

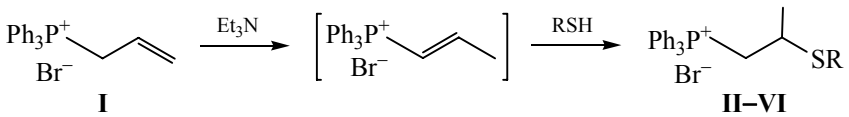
As can be seen from the scheme, prototropic isomerization of the phosphonium salt **I** by the action of amine followed by the addition of RSH to the formed α,β-double bond gives rise to phosphonium salts **II**–**VI** with over 80% yields. Triphenyl-2-(β-dimethylaminoethylsulfanyl)propylphosphonium bromide **V** was obtained with the lowest yield (72%) (Scheme 1).

Taking into account regularities of the alkaline hydrolysis of quaternary phosphonium salts and the anionization of the most anion-labile radical, it may be presumed that the resulting salts **II**–**VI** can be convenient synthons for obtaining 2-(alkylsulfanyl)-propyldiphenylphosphine oxides containing an asymmetric carbon atoms and potentially practically interesting.

The first experiments showed that the phosphonium salts **II** and **VI** react with a two-fold amount of potassium *tert*-butoxide in THF at room temperature to give the expected phosphine oxides **VII** (47%) and **VIII** (45%) as a result of alkaline hydrolysis. In addition, in both cases diphenylpropenylphosphine oxide **IX** was obtained with 28 and 40% yield, respectively, as the product of competitive reaction (1,2-cleavage) (Scheme 2).

The yields of target phosphines **VII** and **VIII** increased (61 and 56%, respectively) with decrease in the reaction temperature (–5 to –7°C); in addition, the

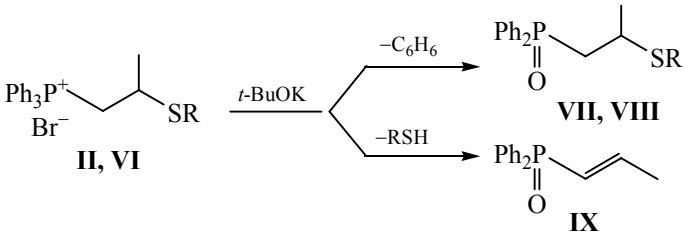
Scheme 1.



I **II–VI**

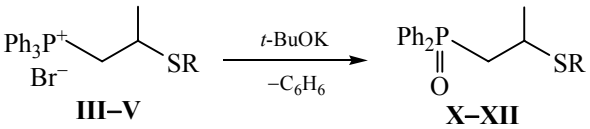
R = Et (**II**), Bu (**III**), *tert*-C_5H_{11} (**IV**), $CH_2CH_2N(CH_3)_2$ (**V**), CH_2CH_2OH (**VI**).

Scheme 2.



R = C_2H_5 (**II, VII**), CH_2CH_2OH (**VI, VIII**).

Scheme 3.



R = C_4H_9 (**III, X**), *tert*-C_5H_{11} (**IV, XI**), $CH_2CH_2N(CH_3)_2$ (**V, XII**).

yield of phosphine oxide **IX** reduced to 15 and 26%, respectively.

Alkaline hydrolysis of the phosphonium salts **III**–**V** with potassium *tert*-butoxide under the same conditions resulted only in the tertiary phosphine oxides **X**–**XII** containing alkyl- or (β-dimethylamino) ethylsulfanyl group (Scheme 3).

Thus our research shows that an increase in the reaction temperature and higher mobility of anionic substituent at the sulfur atom favor 1,2-cleavage, and conversely, lower temperature and the presence of alkyl substituents at the sulfur atom favor the formation of 2-(alkylsulfanyl)propyldiphenylphosphine oxides.

EXPERIMENTAL

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

All reactions were performed in a 50 mL three-necked flask equipped with a mechanical stirrer, reflux condenser, dropping funnel, and gas inlet. Allyltriphenylphosphonium bromide **I** was obtained by a known method [4].

Triphenyl-[2-(ethylsulfanyl)propyl]phosphonium bromide (II). A mixture of 1.5 g (3.9 mmol) of salt **I**, 0.4 g (3.9 mmol) of triethylamine, and 0.24 g (3.9 mmol) of ethanethiol in 20 mL of chloroform was stirred at room temperature for 24 h. Chloroform was removed, and the residue was washed with benzene and anhydrous diethyl ether, then dried in a vacuum. Yield 1.55 g (89.1%), mp 101–103°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 t (3H, SCH_2CH_3, *J* 7.4), 1.4 d.d (3H, CH_3CH, J_1 6.7, J_2 1.5), 2.45 q (2H, $SC\underline{H}_2CH_3$, *J* 7.4), 3.09–3.2 m (1H, CH), 4.05–4.25 m (2H, P^+CH_2), 7.65–8.0 m (15H, P^+Ph_3). ^{31}P NMR spectrum: δ_P 26.94 ppm. Found, %: Br 17.55; P 6.78. $C_{23}H_{26}BrPS$. Calculated, %: Br 17.97; P 6.97.

2-(Butylsulfanyl)propyltriphenylphosphonium bromide (III) was obtained similarly from 1.5 g (3.9 mmol) of salt **I**, 0.4 g (3.9 mmol) of triethylamine and 0.35 g (3.9 mmol) of *n*-butanethiol in 20 mL of chloroform. Yield 1.67 g (90.8%), mp 124–126°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.88 t (3H, CH_2CH_3, *J* 7.1), 1.35 d.d (3H, CH_3CH, J_1 6.9, J_2 1.7), 1.25–1.45 m (4H, $CH_2CH_2CH_3$), 2.47 t (2H, $SC\underline{H}_2CH_2$, *J* 7.3), 3.1–3.21 m (1H, CH), 4.1–4.2 m (2H, P^+CH_2), 7.45–7.9 m (15H, P^+Ph_3). ^{31}P NMR spectrum: δ_P 27.13 ppm. Found, %: Br 17.24; P 6.32. $C_{25}H_{30}BrPS$. Calculated, %: Br 16.91; P 6.55.

2-(1,1-Dimethylpropylsulfanyl)propyltriphenylphosphonium bromide (IV) was obtained similarly from 1.5 g (3.9 mmol) of salt **I**, 0.4 g (3.9 mmol) of triethylamine and 0.41 g (3.9 mmol) of 1,1-dimethylpropanethiol in 20 mL of chloroform. Yield 1.56 g (82.2%), mp 133–135°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_2CH_3, *J* 7.1), 1.02 s and 1.03 s [6H, $C(CH_3)_2$], 1.36 d.d (3H, CH_3CH, J_1 6.8, J_2 1.6), 1.42 q (2H, CH_2CH_3, *J* 7.4), 3.08–3.19 m (1H, CH),

4.0–4.15 m (2H, P^+CH_2), 7.6–7.9 m (15H, P^+Ph_3). ^{31}P NMR spectrum: δ_P 26.87 ppm. Found, %: Br 16.78; P 6.64. $C_{26}H_{32}BrPS$. Calculated, %: Br 16.43; P 6.37.

2-(2-Dimethylaminoethylsulfanyl)propyltriphenylphosphonium bromide (V). To a mixture of 0.53 g (5.2 mmol) of triethylamine and 1 g (2.6 mmol) of salt **I** in 10 mL of chloroform was added dropwise a solution of 0.36 g (2.6 mmol) of *N*,*N*-dimethyl-2-sulfanylethylammonium chloride in 10 mL of chloroform. The reaction mixture was stirred at room temperature for 20 h, and then treated with diluted aqueous sodium carbonate solution. The organic layer was separated, dried over $MgSO_4$, filtered, and evaporated. The residue was washed with benzene and anhydrous diethyl ether, dried in a vacuum. Yield 0.91 g (72%), mp 165–167°C. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.42 d.d (3H, CH_3, J_1 6.6, J_2 1.5), 2.45 br. s [6H, N$(CH_3)_2$], 2.61–2.81 m (4H, SCH_2CH_2N), 3.06 m (1H, CH), 4.11–4.30 m (2H, P^+CH_2), 7.71–7.79 m (6H, P^+Ph), 7.82–7.89 m (3H, P^+Ph), 7.92–8.02 m (6H, P^+Ph). ^{31}P NMR spectrum: δ_P 27.83 ppm. Found, %: Br 15.98; N 3.01; P 6.56. $C_{25}H_{31}BrNPS$. Calculated, %: Br 16.39; N 2.87; P 6.35.

2-(2-Hydroxyethylsulfanyl)propyltriphenylphosphoniumbromide (VI). A mixture of 0.4 g (3.9 mmol) of triethylamine and 0.3 g (3.9 mmol) of 2-sulfanylethanol was added dropwise to a solution of 1.5 g (3.9 mmol) of the salt **I** in 20 mL of chloroform. The reaction mixture was refluxed for 8 h. After the solvent removal in a vacuum the residue was washed with benzene and anhydrous diethyl ether, and then dried in a vacuum. Yield 1.59 g (88.4%), mp 170–173°C. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.4 d.d (3H, CH_3, J_1 6.7, J_2 1.5), 2.55 t (2H, SCH_2, *J* 7.3), 3.02–3.19 m (1H, CH), 3.4 t.d (2H, OCH_2, J_1 7.1, J_2 7.1), 4.0–4.18 m (2H, P^+CH_2), 4.65 t (1H, OH, *J* 7.1), 7.65–7.8 m (6H, P^+Ph), 7.8–8.0 m (9H, P^+Ph). ^{31}P NMR spectrum: δ_P 27.76 ppm. Found, %: Br 17.52; P 6.41. $C_{23}H_{26}BrOPS$. Calculated, %: Br 17.35; P 6.72.

Diphenyl-2-(ethylsulfanyl)propylphosphine oxide (VII). *a*. To a suspension of 1.2 g (2.7 mmol) of salt **II** in 20 mL of anhydrous THF was added 0.6 g (5.4 mmol) of potassium *tert*-butoxide under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 5 h. Then the solution was filtered, and the residue was twice treated with anhydrous THF. Combined tetrahydrofuran extracts were evaporated in a vacuum. The residue was washed with anhydrous benzene and dried in a vacuum. Yield 0.39 g (47.2%). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.12 t (3H, CH_3CH_2, *J* 7.4), 1.31 d (3H, CH_3CH, *J* 6.7), 2.42 d.d.d (1H, PCH_2, J_1 15.0, J_2 11.5, J_3 10.4), 2.48 q (2H, SCH_2, *J* 7.4), 2.66 d.d.d (1H, PCH_2, J_1 15.0, J_2 10.5, J_3 3.1), 3.01–3.12 m (1H, CH), 7.41–7.82 m (10H, PPh_2). ^{31}P NMR spectrum: δ_P 31.65 ppm. Found, %: C 67.34; H 6.91; P 10.26. $C_{17}H_{21}OPS$. Calculated, %: C 67.11; H 6.91; P 10.19.

Diphenylpropenylphosphine oxide **IX** was isolated from the benzene extract. Yield 0.18 g (27.5%), mp 113–114°C. The substance showed no melting point depression when mixed with an authentic sample [6].

b. Phosphine oxide **VII** was obtained similarly from 1.2 g (2.7 mmol) of the salt **II** and 0.6 g (5.4 mmol) of potassium *tert*-butoxide in 20 mL of anhydrous THF at –5 to –7°C. Yield 0.5 g (61.1%) (^1H and ^{31}P NMR data coincided with those of an authentic sample). Additionally, 0.1 g (15.3%) of phosphine oxide **IX** was obtained.

2-(2-Hydroxyethylsulfanyl)propyldiphenylphosphine oxide (VIII) was obtained similarly (method *a*) from 1.5 g (3.3 mmol) of salt **VI** and 0.73 g (6.5 mmol) of potassium *tert*-butoxide in 25 mL of anhydrous THF. Yield 0.48 g (45.5%). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.3 d (3H, CH_3, *J* 6.8), 2.4–2.6 m (3H, SCH_2, PCH_2), 2.78 d.d.d (1H, PCH_2, J_1 13.5, J_2 10.2, J_3 3.0), 3.05–3.2 m (1H, CH), 3.45 t.d (2H, OCH_2, J_1 7.3, J_2 7.1), 7.4–7.85 m (10H, PPh_2). ^{31}P NMR spectrum: δ_P 31.99 ppm. Found, %: C 64.02; H 6.93; P 9.37. $C_{17}H_{21}O_2PS$. Calculated, %: C 63.75; H 6.56; P 9.68. Additionally, 0.32 g (40.1%) of phosphine oxide **IX** was obtained.

b. Phosphine oxide **VIII** was obtained similarly from 1.5 g (3.3 mmol) of salt **VI** and 0.73 g (6.5 mmol) of potassium *tert*-butoxide in 25 mL of anhydrous THF. Yield 0.6 g (56.8%) ^1H and ^{31}P NMR data coincided with those of an authentic sample). Additionally, 0.2 g (26.3%) of the phosphine oxide **IX** was obtained.

2-**(Butylsulfanyl)propyldiphenylphosphine oxide (X)** was obtained similarly using method *b* from 1.0 g (2.1 mmol) of salt **III** and 0.47 g (4.2 mmol) of potassium *tert*-butoxide in 20 mL of anhydrous THF. Yield 0.54 g (77.5%). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.87 t (3H, CH_3CH_2, *J* 7.1), 1.32 d (3H, CH_3CH, *J* 6.7), 1.28–1.46 m (4H, $CH_2CH_2CH_3$), 2.35–2.48 m (3H, PCH_2, SCH_2), 2.66 d.d.d (1H, PCH_2, J_1 13.4, J_2 10.3, J_3 3.2), 2.97–3.08 m (1H, CH), 7.43–7.81 m (10H, PPh_2). ^{31}P NMR spectrum: δ_P 31.83 ppm.

Found, %: C 68.33; H 7.32; P 9.78. $C_{19}H_{25}OPS$. Calculated, %: C 68.67; H 7.53; P 9.34.

2-(1,1-Dimethypropylsulfanyl)propyldiphenylphosphine oxide (XI) was obtained similarly from 1.33 g (2.7 mmol) of salt **IV** and 0.6 g (5.4 mmol) of potassium *tert*-butoxide in 25 mL of anhydrous THF. Yield 0.66 g (70.6%). ^{1}H NMR, δ, ppm (*J*, Hz): 0.85 t (3H, CH_3CH_2, *J* 7.4), 1.06 s and 1.07 s [6H, $C(CH_3)_2$], 1.32 d (3H, CH_3CH, *J* 6.8), 1.4 q (2H, CH_3CH_2, *J* 7.4), 2.5 d.d.d (1H, PCH_2, J_1 15.0, J_2 11.5, J_3 10.3), 2.65 d.d.d (1H, PCH_2, J_1 15.0, J_2 10.4, J_3 3.0), 3.01–3.18 m (1H, CH), 7.41–7.8 m (10H, PPh_2). ^{31}P NMR spectrum: δ_P 31.21 ppm. Found, %: C 69.04; H 7.62; P 9.13. $C_{20}H_{27}OPS$. Calculated, %: C 69.36; H 7.80; P 8.96.

2-(2-Dimethylaminoethylsulfanyl)propyldiphenylphosphine oxide (XII) was obtained similarly from 1.28 g (2.6 mmol) of salt **V** and 0.59 g (5.2 mmol) of potassium *tert*-butoxide in 25 mL of anhydrous THF. Yield 0.64 g (70.9%). ^{1}H NMR, δ, ppm (*J*, Hz): 1.4 d (3H, CH_3, *J* 6.7), 2.15 s [6H, $N(CH_3)_2$], 2.25 d.d.d (1H, PCH_2, J_1 15.1, J_2 11.3, J_3 10.2), 2.32–2.40 m (4H, SCH_2CH_2N), 2.50 d.d.d (1H, PCH_2, J_1 15.1, J_2 10.4, J_3 2.9), 3.0–3.1 m (1H, CH), 7.4–7.8 m (10H, PPh_2). ^{31}P NMR spectrum: δ_P 31.64 ppm. Found, %: C 65.46; H 7.14; P 9.16. $C_{19}H_{26}ONPS$. Calculated, %: C 65.71; H 7.49; P 8.93.

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