Synthesis of 1,2-azaphospholanes containing an amino acid fragment

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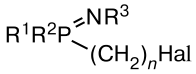
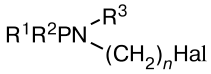
2-Oxo-1,2-azaphospholanes and 1,2-azaphospholanium salts containing an amino acid fragment were synthesized by intramolecular P-alkylation of *N*-3-chloropropyl-substituted tricoordinate phosphorus amides. Hydrolysis of 2-oxo-1,2-azaphospholanes at the P—N bond gives rise to γ-aminopropylphosphonic acid derivatives.

Key words: P-alkylation, Arbuzov rearrangement, 2-oxo-1,2-azaphospholanes, 1,2-azaphospholanium salts, diastereomers, hydrolysis, γ-aminopropylphosphonic acid derivatives, NMR spectroscopy, X-ray diffraction study.

Earlier,[1] we have developed a general approach to the synthesis of poorly studied 1,2-azaphospholanes, which are difficult to prepare, based on intramolecular *N*-alkylation of ω-haloalkyl-substituted iminophosphoryl compounds **I**. More recently,[2] a simpler and more convenient procedure has been proposed for the synthesis of 1,2-azaphospholanes based on intramolecular P-alkylation of *N*-ω-haloalkyl-substituted tricoordinate phosphorus amides **II**.



I



II

In the present study, we used this method to synthesize new types of 1,2-azaphospholanes containing an amino acid fragment with the aim of preparing potent biologically active compounds.

The reactions of tricoordinate phosphorus acid chlorides **1a—c** with *N*-3-chloropropylglycine ethyl ester (**2a**) or DL-*N*-3-chloropropylalanine ethyl ester (**2b**) in the presence of triethylamine in a 2 : 1 C_6H_6—$CHCl_3$ solvent mixture or in MeCN produced *N*-3-chloropropyl-substituted amides **3a—e** (Scheme 1), whose signals were observed in the ^{31}P NMR spectra of the reaction mixtures (see the Experimental section). After refluxing of the reaction mixture for 1—4 h, amides **3** were transformed into 1,2-azaphospholanes **4** and **5** as a result of intramolecular P-alkylation.

The P-alkylation of amidophosphites **3a—c** containing the ethoxy substituent at the phosphorus atom occurs as the Arbuzov rearrangement. Under the reaction conditions, the intermediate quasiphosphonium salt generated in the first step undergoes dealkylation to give 2-oxo-1,2-azaphospholanes **4a—c**. Intramolecular P-alkylation of aminophosphines **3d,e** containing two phenyl substituents at the phosphorus atom afforded 1,2-azaphospholanium chlorides **5a,b**, from which the corresponding perchlorates **6a,b** were generated by the anion exchange reaction. 2-Oxo-1,2-azaphospholanes **4a—c** and perchlorate **6b** are nondistillable oily liquids, which were purified by column chromatography. 1,2-Azaphospholanium salts **5a** and **6a** were purified by recrystallization (Table 1).

The compositions and structures of compounds **4—6** were confirmed by elemental analysis, IR spectroscopy, and ^1H, ^{31}P, and ^{13}C NMR spectroscopy (Tables 1—3). The IR spectra of all compounds show an absorption band of the C=O group at 1730—1740 cm^{-1}. The IR spectra of 2-oxo-1,2-azaphospholanes **4a—c** have also an intense absorption band of the P=O group at 1200—1230 cm^{-1}. According to the NMR spectra, alanine derivatives **4b,c** were prepared as mixtures of two diastereomers **A** and **B** in a ratio of 1 : 1.* Diastereomers of azaphospholane **4b** were separated by column chromatography on SiO_2.

2-Oxo-1,2-azaphospholanes **4a,b** are easily hydrolyzed at the P—N bond of the ring at 20 °C in the presence of traces of moisture to give compounds **7a,b** (Scheme 2), which are derivatives not only of γ-aminophosphonic acid but also of α-aminocarboxylic acid and can possess useful biological properties.[3,4]

Hydrolysis products **7a,b** were isolated and characterized (see Tables 1—3) as crystalline compounds. Their IR spectra show absorption bands characteristic of the C=O group along with broad intense absorption bands at

* The diastereomer, whose signal in the ^{31}P—$\{^1H\}$ NMR spectrum is observed at lower field, is denoted as **A**.

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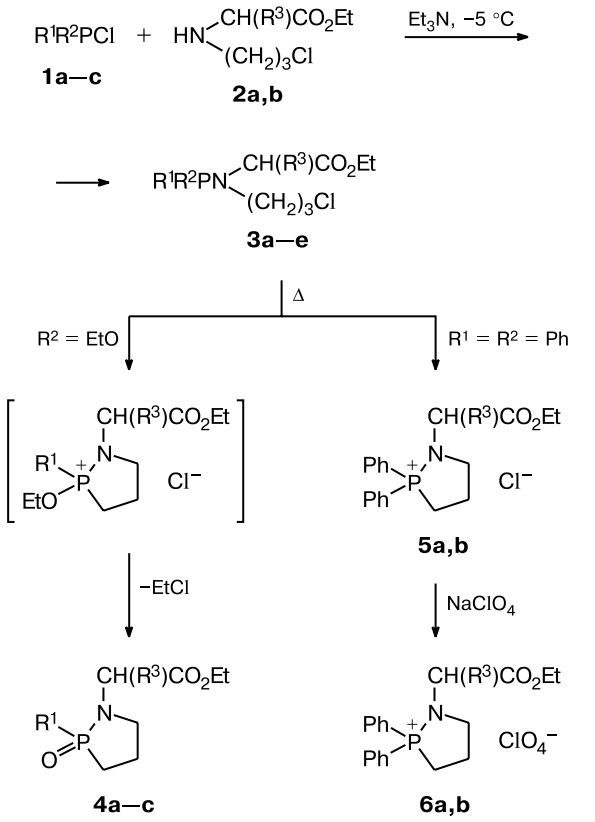
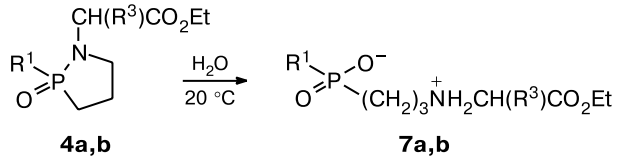
Scheme 1



Compound	R^1	R^2	R^3	Compound	R^1	R^2	R^3
1a	EtO	EtO	—	**3c**	Et_2N	EtO	Me
1b	Et_2N	EtO	—	**3d**	Ph	Ph	H
1c	Ph	Ph	—	**3e**	Ph	Ph	Me
3a	EtO	EtO	H	**4a**	EtO	—	H
3b	EtO	EtO	Me	**4b**	EtO	—	Me
				4c	Et_2N	—	Me

R^3 = H (**2a**, **5a**, **6a**); Me (**2b**, **5b**, **6b**)

Scheme 2



R^1 = EtO, R^3 = H (**a**); EtO, Me (**b**)

3700—2000 cm^{-1} belonging to the NH_2^+ group and absorption bands at 1200—1000 cm^{-1} assigned to vibrations of the P—O—C and PO_2^- groups (see Table 2), which is evidence that these compounds exist as zwitterions.[5—7] In the ^1H NMR spectra of the hydrolysis products in $CDCl_3$, the signal for the proton of the NH group is absent, and a very broad singlet for the protons of the NH_2^+ group is observed at δ 10—11 (ν ≈ 1000 Hz (**7a**) and 550 Hz (**7b**)).

X-ray diffraction study demonstrated that compound **7a** crystallizes in the zwitterionic form with a chloroform solvate molecule (Table 4, Fig. 1). The phosphorus atom is characterized by a distorted tetrahedral coordination. The O(2)—P(1)—O(1) bond angle is increased to 118.2(1)° and is synclinal with respect to the C(1)C(2)C(3)N(1)C(4)C(5) fragment (the C(3)—C(2)—C(1)—P(1) torsion angle is 87.3°). The PO_2OEt group is arranged with respect to the alkylene chain in such a way that the O(1) and O(3) atoms are synclinal, whereas the O(2) atom is antiperiplanar with respect to the C(2) atom.

The P(1)—O(1) and P(1)—O(2) bonds in **7a** are similar in length. A slight elongation of the P(1)—O(2) bond (1.503(2) Å) compared to the P(1)—O(1) bond (1.486(2) Å) is, apparently, associated with the difference in both the strength and number of H bonds formed by the oxygen atoms. Although both the O(1) and O(2) atoms are involved in intermolecular N—H...O hydrogen bonds

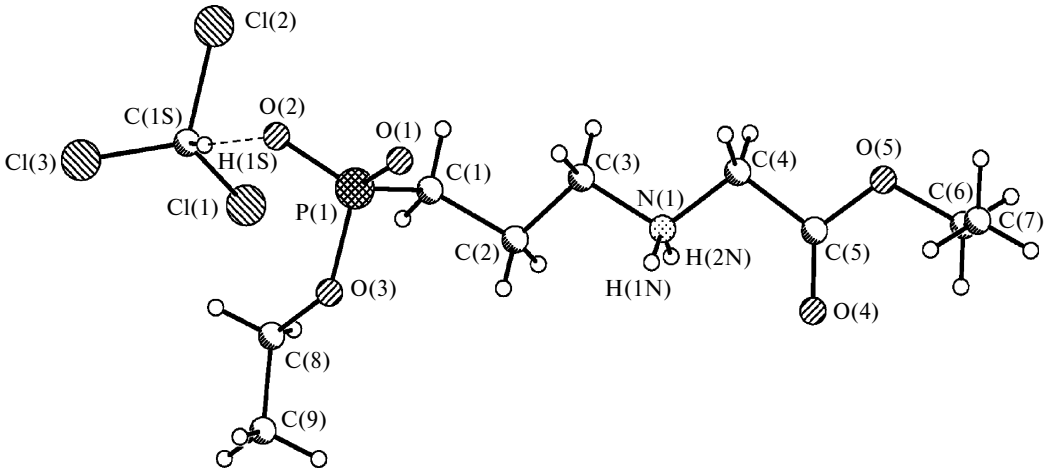


Fig. 1. Crystal structure of compound **7a** · $CHCl_3$.

Table 1. Yields, melting points, and elemental analysis data for 2-oxo-1,2-azaphospholanes **4**, 1,2-azaphospholanium salts **5** and **6**, and hydrolysis products **7**

Compound	Yield[a] (%)	M.p./°C (solvent)	Found / Calculated (%)				Molecular formula
			C	H	N	P	
4a	60.0[b] (84)	—	46.04	7.56	6.03	13.14	$C_9H_{18}NO_4P$
			45.95	7.66	5.95	13.19	
4b	68.0[b] (88)	—	48.69	8.01	5.64	11.95	$C_{10}H_{20}NO_4P$
			48.19	8.03	5.62	12.45	
4c	58.8[b] (76)	—	52.25	8.98	10.03	11.17	$C_{12}H_{25}N_2O_3P$
			52.17	9.06	10.14	11.23	
5a[c]	38.3 (87)	160—161 (decomp.) (MeCN—AcOEt)	62.64	6.40	3.70	8.42	$C_{19}H_{23}ClNO_2P$
			62.72	6.37	3.85	8.51	
6a[d]	58.6	120—121 (decomp.) (CH_2Cl_2—AcOEt)	53.38	5.30	3.26	7.44	$C_{19}H_{23}ClNO_6P$
			53.34	5.42	3.27	7.24	
6b	47.7[b]	—	53.79	5.98	3.01	7.07	$C_{20}H_{25}ClNO_6P$
			54.36	5.66	3.17	7.02	
7a	78 (quantitative)	157—158 (MeCN—AcOEt)	42.52	8.01	5.41	12.08	$C_9H_{20}NO_5P$
			42.69	7.91	5.53	12.25	
7b	88 (quantitative)	126—128 (MeCN—AcOEt)	44.89	8.21	5.21	11.63	$C_{10}H_{22}NO_5P$
			44.94	8.23	5.24	11.61	

[a] The yield of the pure product; the yield of the product, which was determined from the ^{31}P NMR spectrum of the reaction mixture, is given in parentheses.
[b] Purified by column chromatography.
[c] Found (%): Cl, 9.68. Calculated (%): Cl, 9.75.
[d] Found (%): Cl, 8.38. Calculated (%): Cl, 8.29.

(O...N, 2.677(2) and 2.720(2) Å, respectively), the O(2) atom forms also a strong H bond with the chloroform molecule (H(1S)...O(2), 1.97 Å; C(1S)...O(2), 3.031(2) Å; C(1S)—H(1S)...O(2), 166°). In the crystal structure, the molecules are linked to each other by N—H...O hydrogen bonds to form layers parallel to the crystallographic *bc* plane, and the chloroform solvate molecules form a hydrophilic coat.

Experimental

The reactions were carried out under dry argon using anhydrous solvents. The NMR spectra were recorded on a Bruker AMX-400 instrument with the use of the signal from the residual protons of a deuterated solvent ($CDCl_3$) as the internal standard (^1H and ^{13}C) and 85% H_3PO_4 as the external standard (^{31}P). The IR spectra were measured on Magna IR 750 Nicolet and UR-20 instruments in a thin film or in KBr pellets. The syntheses were carried out with the use of the commercial reagents $(EtO)_2PCl$, Ph_2PCl (Aldrich), and $Cl(CH_2)_3NH_2 \cdot HCl$ (Acros). Column chromatography was performed on SiO_2 (Aldrich, 130—270 mesh) using gradient elution with a hexane—acetone or $CHCl_3$—MeOH mixture. The starting $(EtO)(Et_2N)PCl$ was synthesized according to a known procedure.[8]

Ethyl *N*-3-chloropropylaminoacetate (2a). A solution of $Cl(CH_2)_3NH_2 \cdot HCl$ (3.00 g, 22.8 mmol), Et_3N (2.3 g, 22.8 mmol), and $BrCH_2COOEt$ (1.90 g, 11.4 mmol) in EtOH (20 mL) was stirred at 20 °C for 3 days. The precipitate was filtered off, and the filtrate was concentrated to dryness. Benzene (20 mL) and ice water (20 mL) were added to the residue. The benzene layer was dried with Na_2SO_4, the solvent was removed *in vacuo*, and the oily residue was purified by column chromatography (hexane—acetone as the eluent; a gradient from 98 : 2 to 90 : 10). The yield was 1.12 g (54.6%). Found (%): C, 46.72; H, 8.00; N, 7.90; Cl, 19.65. $C_7H_{14}ClNO_2$. Calculated (%): C, 46.80; H, 7.80; N, 7.80; Cl, 19.78. IR (thin film), ν/cm^{-1}: 1737 (C=O); 3340 (NH). ^1H NMR ($CDCl_3$), δ: 1.21 (t, 3 H, CH_3, $^3J_{H,H}$ = 7.2 Hz); 1.55 (br.s, 1 H, NH); 1.89 (tt, 2 H, $CH_2C\underline{H}_2CH_2$, $^3J_{H,H}$ = 6.8 Hz); 2.72 (t, 2 H, $CH_2C\underline{H}_2N$, $^3J_{H,H}$ = 6.8 Hz); 3.35 (s, 2 H, CH_2CO); 3.58 (t, 2 H, CH_2Cl, $^3J_{H,H}$ = 6.8 Hz); 4.12 (q, 2 H, CH_2O, $^3J_{H,H}$ = 7.2 Hz).

Ethyl DL-*N*-3-chloropropyl-2-aminopropionate (2b) was synthesized analogously from $Cl(CH_2)_3NH_2 \cdot HCl$ (3.00 g, 22.8 mmol), Et_3N (2.30 g, 22.8 mmol), and DL-BrCH(Me)COOEt (2.10 g, 11.4 mmol). Column chromatography afforded an oily product in a yield of 1.45 g (65.5%). Found (%): C, 49.59; H, 8.38; N, 7.42. $C_8H_{16}ClNO_2$. Calculated (%): C, 49.61; H, 8.27; N, 7.24. IR (thin layer), ν/cm^{-1}: 1725 (C=O); 3330 (NH). ^1H NMR ($CDCl_3$), δ: 1.18—1.28 (m, 6 H, $C\underline{H}_3CH_2$ + $C\underline{H}_3CH$); 1.45 (br.s, 1 H, NH); 1.81—1.93 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.52—2.61 and 2.67—2.76 (both m, 2 H, $CH_\alpha H_\beta N$); 3.22—3.30 (m, 1 H, $C\underline{H}CH_3$); 3.52—3.62 (m, 2 H, CH_2Cl); 4.12 (q, 2 H, CH_2O, $^3J_{H,H}$ = 7.2 Hz).

2-Ethoxy-1-ethoxycarbonylmethyl-2-oxo-1,2λ^5-azaphospholane (4a). A solution of $(EtO)_2PCl$ (0.73 g, 4.6 mmol) in MeCN (5 mL) was added dropwise with stirring to a solution of **2a** (1.0 g, 5.6 mmol) and Et_3N (0.57 g, 5.6 mmol) in MeCN (15 mL) cooled to −5 °C. After completion of stirring, the

Table 2. ^{31}P and ^{13}C NMR spectra of compounds **4—7** in $CDCl_3$

Compound	NMR, δ ($J_{C,P}$/Hz)	
	$^{31}P—\{^1H\}$	^{13}C
4a	46.8	13.41 (s, $\underline{C}H_3CH_2OC$); 15.73 (d, $\underline{C}H_3CH_2OP$, J = 6.2); 18.61 (d, $CH_2\underline{C}H_2CH_2$, J = 1.8); 20.02 (d, CH_2P, J = 120.7); 45.09 (d, $\underline{C}H_2CO$, J = 4.4); 46.46 (d, $NCH_{2,cycle}$, J = 24.2); 60.06 (s, $\underline{C}H_2OC$); 60.40 (d, CH_2OP, J = 6.5); 169.5 (d, CO, J = 2.9)
4b (**A**)	47.3	13.89 (s, $\underline{C}H_3CH_2OC$); 16.06 (d, $\underline{C}H_3CH$, J = 2.8); 16.27 (d, $\underline{C}H_3CH_2OP$, J = 6.0); 19.30 (d, $CH_2\underline{C}H_2CH_2$, J = 2.4); 21.02 (d, CH_2P, J = 120.0); 42.43 (d, $NCH_{2,cycle}$, J = 24.4); 51.08 (d, CH, J = 4.0); 60.63 (s, $\underline{C}H_2OC$); 61.12 (d, CH_2OP, J = 6.0); 172.40 (d, CO, J = 3.5)
4b (**B**)	46.4	13.89 (s, $\underline{C}H_3CH_2OC$); 15.78 (d, $\underline{C}H_3CH$, J = 2.8); 16.21 (d, $\underline{C}H_3CH_2OP$, J = 5.2); 19.40 (d, $CH_2\underline{C}H_2CH_2$, J = 2.4); 20.88 (d, CH_2P, J = 120.4); 41.81 (d, $NCH_{2,cycle}$, J = 24.9); 50.28 (d, CH, J = 4.4); 60.52 (s, $\underline{C}H_2OC$); 61.50 (d, CH_2OP, J = 5.6); 172.60 (d, CO, J = 3.5)
4c	45.9 (**A**), 45.3 (**B**)	14.56, 14.64 (both s, $\underline{C}H_3CH_2O$); 16.53 (s, $\underline{C}H_3CH$); 17.02 (s, $\underline{C}H_3CH_2N$); 21.12, 21.44 (both s, $CH_2\underline{C}H_2CH_2$); 23.03, 23.23 (both d, CH_2P, J = 107.7); 38.54, 38.72 (both d, $CH_3\underline{C}H_2N$, J = 4.7); 42.13, 44.16 (both d, $NCH_{2,cycle}$, J = 23.7, J = 22.8); 49.99, 51.10 (both s, CH); 61.25, 61.32 (both s, CH_2O); 173.5 (s, CO)
5a	60.0	13.64 (s, CH_3); 21.67 (s, $CH_2\underline{C}H_2CH_2$); 26.50 (d, CH_2P, J = 65.1); 47.20 (d, $\underline{C}H_2CO$, J = 4.4); 52.88 (d, $NCH_{2,cycle}$, J = 15.6); 61.48 (s, CH_2O); 119.10 (d, P—C(Ph), J = 95.21); 129.90 (d, *m*-C(Ph), J = 13.3); 133.20 (d, *o*-C(Ph), J = 12.1); 135.10 (d, *p*-C(Ph), J = 2.8); 168.60 (s, CO)
6a	59.2	13.80 (s, CH_3); 21.63 (s, $CH_2\underline{C}H_2CH_2$); 26.11 (d, CH_2P, J = 66.0); 47.06 (d, $\underline{C}H_2CO$, J = 3.9); 52.80 (d, $NCH_{2,cycle}$, J = 15.8); 61.73 (s, CH_2O); 119.20 (d, P—C(Ph), J = 95.4); 130.10 (d, *m*-C(Ph), J = 13.5); 133.20 (d, *o*-C(Ph), J = 11.9); 135.40 (d, *p*-C(Ph), J = 2.8); 168.60 (d, CO, J = 3.3)
6b	57.2	12.78 (s, $\underline{C}H_3CH_2$); 16.87 (s, $\underline{C}H_3CH$); 21.06 (s, $CH_2\underline{C}H_2CH_2$); 25.18 (d, CH_2P, J = 66.3); 47.66 (d, NCH_2, J = 16.1); 52.13 (s, CH); 61.34 (s, CH_2O); 119.3 (d, P—C(Ph), J = 97.2); 119.40 (d, P—C(Ph), J = 94.8); 129.80 (d, *m*-C(Ph), J = 13.5); 132.90 (d, *o*-C(Ph), J = 11.8); 135.00 (d, *p*-C(Ph), J = 2.8); 170.50 (d, CO, J = 1.4)
7a	24.3	13.60 (s, $\underline{C}H_3CH_2OC$); 16.40 (d, $\underline{C}H_3CH_2OP$, J = 6.3); 20.58 (d, $CH_2\underline{C}H_2CH_2$, J = 4.0); 24.91 (d, CH_2P, J = 135.0); 47.30 (s, $\underline{C}H_2CO$); 48.91 (d, $CH_2\underline{C}H_2N$, J = 10.0); 60.21 (d, CH_2OP, J = 5.5); 62.60 (s, $\underline{C}H_2OC$); 167.10 (s, CO)
7b	23.1	13.61 (s, $\underline{C}H_3CH_2OC$); 14.47 (s, $\underline{C}H_3CH$); 16.45 (d, $\underline{C}H_3CH_2OP$, J = 6.4); 20.88 (d, $CH_2\underline{C}H_2CH_2$, J = 4.0); 25.01 (d, CH_2P, J = 135.0); 47.28 (d, $CH_2\underline{C}H_2N$, J = 11.0); 55.45 (s, CH); 60.19 (d, CH_2OP, J = 5.4); 62.77 (s, $\underline{C}H_2OC$); 170.00 (s, CO)

reaction mixture contained 84% of amide **3a** (^{31}P NMR spectroscopic data), δ_P 146.4.* The reaction mixture was refluxed for 2 h and cooled. The precipitate of $Et_3N \cdot HCl$ was filtered off, MeCN was removed *in vacuo*, benzene (20 mL) was added to the filtrate, the precipitate of $Et_3N \cdot HCl$ was filtered off, benzene was removed *in vacuo*, and the oily product was purified by chromatography (hexane—acetone as the eluent; a gradient from 98 : 2 to 45 : 55). Compound **4a** was isolated in a yield of 0.65 g.

2-Ethoxy-1-(1-ethoxycarbonylethyl)-2-oxo-1,2λ^5-azaphospholane (4b). A solution of $(EtO)_2PCl$ (1.25 g, 8.0 mmol) in a 2 : 1 C_6H_6—$CHCl_3$ mixture (5 mL) was added dropwise with stirring to a solution of **2b** (1.55 g, 8.0 mmol) and Et_3N (0.96 g, 9.5 mmol) in the same solvent mixture (25 mL) at −5 °C. The reaction mixture contained 89% of amide **3b**, δ_P 148.4.* Then the reaction mixture was refluxed for 4 h, C_6H_6 (15 mL) and ice water (15 mL) were added, the benzene layer was separated and washed with ice water, the aqueous layer was extracted with C_6H_6, and the benzene extracts were dried with Na_2SO_4. After removal of C_6H_6, the residue was chromatographed on a column (hexane—acetone as the eluent; a gradient from 98 : 2 to 40 : 60). A viscous oily product was obtained as a mixture of two diastereomers of **4b** in a yield of 1.35 g. Diastereomers **A** and **B** were isolated by additional chromatography of the reaction mixture using the same solvents.

2-Diethylamino-1-(1-ethoxycarbonylethyl)-2-oxo-1,2λ^5-azaphospholane (4c) was synthesized analogously to **4b** from **2b** (0.84 g, 4.3 mmol), Et_3N (0.61 g, 6.0 mmol), and $(EtO)(Et_2N)PCl$ (0.79 g, 4.3 mmol) in a 2 : 1 C_6H_6—$CHCl_3$ mixture (15 mL). Before heating, the reaction mixture contained 80% of amide **3c**, δ_P 137.5 and 137.9 (two diastereomers).* Compound **4c** was isolated as a mixture of two diastereomers in a yield of 0.70 g by column chromatography ($CHCl_3$—MeOH as the eluent; a gradient from 100 : 1 to 100 : 8).

1-Ethoxycarbonylmethyl-2,2-diphenyl-1,2λ^4-azaphospholanium chloride (5a) was synthesized analogously to **4b** from **2a** (1.02 g, 5.7 mmol), Et_3N (0.66 g, 6.5 mmol), and Ph_2PCl (1.17 g, 5.3 mmol) in a 2 : 1 C_6H_6—$CHCl_3$ mixture (25 mL). Before heating, the reaction mixture contained 88% of amide **3d**, δ_P 65.0.** After refluxing for 1 h, the precipitate of $Et_3N \cdot HCl$ was filtered off, and the solvent was removed *in vacuo*. After recrystallization, chloride **5a** was isolated in a yield of 0.74 g.

1-Ethoxycarbonylmethyl-2,2-diphenyl-1,2λ^4-azaphospholanium perchlorate (6a). A solution of $NaClO_4$ (0.73 g, 6.0 mmol)

* For $(EtO)_2PNMe_2$, δ_P 144.7.[9]

* For $(EtO)P(NEt_2)_2$, δ_P 133.0.[10]

** For Ph_2PNEt_2, δ_P 60.8.[11]

Table 3. IR and ^{1}H NMR spectra ($CDCl_3$) of compounds **4—7**

Compound	IR, ν/cm^{-1}	^{1}H NMR, δ (J/Hz)
4a	1215 (br.s, P=O), 1744 (C=O)	1.23, 1.25 (both t, 6 H, C<u>H</u>$_3$CH$_2$OP + C<u>H</u>$_3$CH$_2$OC, $^3J_{H,H}$ = 7.2); 1.65—1.82 (m, 2 H, CH$_2$C<u>H</u>$_2$CH$_2$); 1.97—2.16 (m, 2 H, PCH$_2$); 3.00—3.09, 3.20—3.28 (both m, 1 H each, NCH$_\alpha$H$_{\beta,cycle}$, $^2J_{H,H}$ = 15.2); 3.52 (dd, 1 H, NCH$_\beta$CO, $^2J_{H,H}$ = 18.0, $^3J_{P,H}$ = 8.4); 3.86 (dd, 1 H, NCH$_\alpha$CO, $^2J_{H,H}$ = 18.0, $^3J_{P,H}$ = 8.6); 3.93—4.06 (m, 2 H, CH$_2$OP); 4.14 (q, 2 H, CH$_2$OC, $^3J_{H,H}$ = 7.2)
4b (**A**)	1220 (br.s, P=O), 1746 (C=O)	1.14—1.21 (m, 6 H, C<u>H</u>$_3$CH$_2$OP + C<u>H</u>$_3$CH$_2$OC); 1.35 (d, 3 H, C<u>H</u>$_3$CH, $^3J_{H,H}$ = 7.2); 1.60—1.72 (m, 2 H, CH$_2$C<u>H</u>$_2$CH$_2$); 1.84—2.02 (m, 2 H, PCH$_2$); 2.98—3.16 (m, 2 H, NCH$_{2,cycle}$); 3.87—3.98 (m, 3 H, CH$_2$OP); 4.01 (q, 1 H, CH, $^3J_{H,H}$ = 7.2); 4.06 (q, 2 H, CH$_2$OC, $^3J_{H,H}$ = 7.2)
4b (**B**)	1220 (br.s, P=O), 1746 (C=O)	1.14—1.21 (m, 6 H, C<u>H</u>$_3$CH$_2$OP + C<u>H</u>$_3$CH$_2$OC); 1.33 (d, 3 H, C<u>H</u>$_3$CH, $^3J_{H,H}$ = 7.2); 1.60—1.72 (m, 2 H, CH$_2$C<u>H</u>$_2$CH$_2$); 1.84—2.02 (m, 2 H, PCH$_2$); 2.98—3.16 (m, 2 H, NCH$_{2,cycle}$); 3.87—3.98 (m, 3 H, CH$_2$OP); 3.99 (q, 1 H, CH, $^3J_{H,H}$ = 7.2); 4.06 (q, 2 H, CH$_2$OC, $^3J_{H,H}$ = 7.2)
4c (**A**, **B**)	1212 (br.s, P=O), 1742 (C=O)	1.00, 1.03 (both t, 6 H, 2 C<u>H</u>$_3$CH$_2$N, $^3J_{H,H}$ = 7.2); 1.21, 1.22 (both t, 3 H, C<u>H</u>$_3$CH$_2$O, $^3J_{H,H}$ = 7.2); 1.38, 1.39 (both d, 3 H, C<u>H</u>$_3$CH, $^3J_{H,H}$ = 7.2); 1.51—1.65, 1.66—1.81 (both m, 2 H, CH$_2$C<u>H</u>$_2$CH$_2$); 1.82—2.15 (m, 2 H, PCH$_2$); 2.97—3.27 (m, 6 H, 2 CH$_3$C<u>H</u>$_2$N + NCH$_{2,cycle}$); 3.88 (dq, 0.5 H, CH, $^3J_{H,H}$ = 7.2, $^3J_{P,H}$ = 6.8); 4.00 (dq, 0.5 H, CH, $^3J_{H,H}$ = 7.2, $^3J_{P,H}$ = 7.4); 4.09, 4.11 (both q, 2 H, CH$_2$O, $^3J_{H,H}$ = 7.2)
5a	1729 (C=O)	1.15 (t, 3 H, CH$_3$, $^3J_{H,H}$ = 7.2); 2.43—2.54 (m, 2 H, CH$_2$C<u>H</u>$_2$CH$_2$); 3.45 (dt, 2 H, NCH$_{2,cycle}$, $^3J_{H,H}$ = $^3J_{P,H}$ = 7.4); 3.79 (d, 2 H, CH$_2$CO, $^3J_{P,H}$ = 9.4); 3.96—4.02 (m, 2 H, PCH$_2$); 4.08 (q, 2 H, CH$_2$O, $^3J_{H,H}$ = 7.2); 7.65—7.70, 7.75—7.79, 8.02—8.08 (all m, 10 H, 2 Ph)
6a	1090 (br.s, ClO_4^-), 1729 (C=O)	1.13 (t, 3 H, CH$_3$, $^3J_{H,H}$ = 7.2); 2.40—2.50 (m, 2 H, CH$_2$C<u>H</u>$_2$CH$_2$); 3.09 (dt, 2 H, NCH$_{2,cycle}$, $^3J_{H,H}$ = $^3J_{P,H}$ = 7.6); 3.71 (d, 2 H, CH$_2$CO, $^3J_{P,H}$ = 9.6); 3.77—3.82 (m, 2 H, PCH$_2$); 4.05 (q, 2 H, CH$_2$O, $^3J_{H,H}$ = 7.2); 7.65—7.70, 7.77—7.88 (both m, 10 H, 2 Ph)
6b	1100 (br.s, ClO_4^-), 1728 (C=O)	1.13 (t, 3 H, C<u>H</u>$_3$CH$_2$, $^3J_{H,H}$ = 7.2); 1.40 (d, 3 H, C<u>H</u>$_3$CH, $^3J_{H,H}$ = 7.2); 2.35—2.47, 2.48—2.59 (both m, 1 H each, CH$_2$C<u>H</u>$_2$CH$_2$); 3.00—3.09, 3.15—3.26 (both m, 1 H each, NCH$_2$); 3.72—3.82 (m, 2 H, PCH$_2$); 3.91 (dq, 1 H, CH, $^3J_{H,H}$ = 7.2, $^3J_{P,H}$ = 8.0); 4.02 (q, 2 H, CH$_2$O, $^3J_{H,H}$ = 7.2); 7.60—7.73, 7.76—7.89 (both m, 10 H, 2 Ph)
7a	1045, 1070, 1102, 1161 (P—O—C, PO_2^-), 1752 (C=O), 2000—3650 (br.s, NH_2^+)	1.24, 1.26 (both t, 6 H, 2 CH$_3$, $^3J_{H,H}$ = 7.2); 1.65—1.73 (m, 2 H, CH$_2$C<u>H</u>$_2$CH$_2$); 2.11—2.25 (m, 2 H, PCH$_2$); 3.02 (t, 2 H, CH$_2$C<u>H</u>$_2$N, $^3J_{H,H}$ = 6.8); 3.69 (c, 2 H, CH$_2$CO); 3.87 (dq, 2 H, CH$_2$OP, $^3J_{H,H}$ = $^3J_{P,H}$ = 7.2); 4.20 (q, 2 H, CH$_2$OC, $^3J_{H,H}$ = 7.2); 10.36 (br.s, 2 H, NH$_2$)
7b	1047, 1064, 1101, 1134, 1153 (P—O—C, PO_2^-), 1743 (C=O), 2000—3700 (br.s, NH_2^+)	1.21, 1.26 (both t, 6 H, C<u>H</u>$_3$CH$_2$OP + C<u>H</u>$_3$CH$_2$OC, $^3J_{H,H}$ = 7.2); 1.59 (d, 3 H, C<u>H</u>$_3$CH, $^3J_{H,H}$ = 7.2); 1.62—1.74 (m, 2 H, CH$_2$C<u>H</u>$_2$CH$_2$); 2.04—2.27 (m, 2 H, PCH$_2$); 2.96 (t, 2 H, NCH$_2$, $^3J_{H,H}$ = 6.8); 3.72 (q, 1 H, CH, $^3J_{H,H}$ = 7.2); 3.89 (dq, 2 H, CH$_2$OP, $^3J_{H,H}$ = $^3J_{P,H}$ = 7.2); 4.22 (q, 2 H, CH$_2$OC, $^3J_{H,H}$ = 7.2); 11.15 (br.s, 2 H, NH$_2$)

Table 4. Selected bond lengths (d) and bond angles (ω) in the crystal of **7a**

Bond	d/Å	Angle	ω/deg
P(1)—O(1)	1.486(2)	O(1)—P(1)—O(2)	118.2(1)
P(1)—O(2)	1.503(2)	O(1)—P(1)—O(3)	106.1(1)
P(1)—O(3)	1.608(3)	O(2)—P(1)—O(3)	109.3(1)
P(1)—C(1)	1.805(4)	O(1)—P(1)—C(1)	110.1(1)
O(3)—C(8)	1.445(4)	O(2)—P(1)—C(1)	108.1(2)
O(4)—C(5)	1.193(4)	O(3)—P(1)—C(1)	104.1(1)
O(5)—C(5)	1.328(4)	C(8)—O(3)—P(1)	120.0(2)
O(5)—C(6)	1.448(4)	C(5)—O(5)—C(6)	117.9(3)
N(1)—C(4)	1.473(4)	C(4)—N(1)—C(3)	114.2(3)
N(1)—C(3)	1.491(4)		

in MeCN (7 mL) was added to a solution of chloride **5a** in MeCN (5 mL), which was prepared from **2a** (0.50 g, 3.0 mmol), Et_3N (0.30 g, 3.0 mmol), and Ph_2PCl (0.67 g, 3.0 mmol), at 20 °C. The precipitate of NaCl was filtered off, MeCN was distilled off *in vacuo*, the residue was treated in CH_2Cl_2 to remove an excess of $NaClO_4$, the filtrate was concentrated *in vacuo*, and the residue was recrystallized. Perchlorate **6a** was isolated in a yield of 0.75 g.

1-(1-Ethoxycarbonylethyl)-2,2-diphenyl-1,2λ^4-azaphospholanium perchlorate (6b) was synthesized analogously to perchlorate **6a** from **2b** (0.97 g, 5.0 mmol), Et_3N (0.61 g, 6.0 mmol), Ph_2PCl (1.10 g, 5.0 mmol), and $NaClO_4$ (1.22 g, 10.0 mmol). The reaction mixture contained 83% of intermediate aminophosphine **3e**, δ_P 55.0.* The perchlorate was purified by column chromatography (hexane—acetone as the eluent; a gradient from 98 : 2 to 50 : 50). The glassy product was isolated in a yield of 1.05 g.

* For Ph_2PNEt_2, δ_P 60.8.[11]

***O*-Ethyl 3-(*N*-ethoxycarbonylmethyl)aminopropylphosphonate (7a)** and ***O*-ethyl 3-(*N*-1-ethoxycarbonylethyl)aminopropylphosphonate (7b)** were prepared in quantitative yields from azaphospholanes **4a** and **4b** upon storage at 20 °C in the presence of traces of moisture for 7 and 30 days, respectively.

X-ray diffraction study of compound 7a. Crystals of compound **7a** were grown by slow crystallization from a $CHCl_3$—AcOEt mixture. At 110 K, colorless crystals of **7a**·$CHCl_3$ ($C_{10}H_{21}Cl_3NO_5P$) (M = 340.67) are monoclinic, space group $P2_1/c$, a = 13.451(2), b = 9.102(1), c = 14.506(2) Å, β = 100.679(3)°, V = 1745.3(4) Å^3, Z = 4, d_{calc} = 1.773 g cm^{-3}, μ(Mo-Kα) = 5.7 cm^{-1}, F(000) = 962. The intensities of 11332 reflections were measured at 110 K on a Smart 1000 CCD diffractometer (λ(Mo-Kα) = 0.71072 Å, ω scanning technique, $2\theta < 55°$), and 4346 independent reflections (R_{int} = 0.0528) were used in the refinement. The structure was solved by direct methods and calculations of successive electron density maps. Analysis of difference Fourier maps showed that two chlorine atoms in the chloroform solvate molecule are disordered over two positions with occupancies of 0.4 and 0.6. All hydrogen atoms were located from difference electron density maps. The structure was refined against F^2_{hkl} with anisotropic displacement parameters for all nonhydrogen atoms and isotropic displacement parameters for H atoms. The final R factors for **7a** were R_1 = 0.0594 (calculated based on F_{hkl} for 4346 reflections with $I > 2\sigma(I)$), wR_2 = 0.1218, GOOF = 1.048. All calculations were carried out using the SHELXTL 5.10 program package.

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