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New Synthetic Approaches to Development of the Chemistry of Pentaerythritol Bicyclophosphite

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Abstract—Syntheses of the original compact molecular systems were developed and the ways of their practical use were examined. A group of new substances was synthesized on the basis of available pentaerythritol bicyclophosphite and thionophosphate, including respective ammonium salts, phosphocholines, a complex compound of molybdenum, and a hydrophosphoryl compound.

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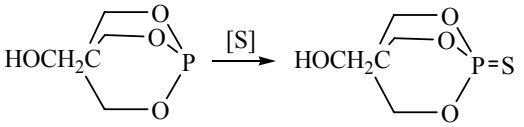
Extending our research in the chemistry of bicyclic esters of phosphorus acids and oligools [1–5], we studied the synthesis of new structures formed on the basis of the transformation of the pentaerythritol phosphobicycles. This work was developed along two lines. The first one is devoted to the study of chemical reactions of cyclic structure of pentaerythritol bicyclophosphite **I**, the second is the study of chemical reactions at the alcohol hydroxyl of the phospho-framework compound and its derivatives. To this end we have performed the sulfurization of the pentaerythritol bicyclophosphite **I**.

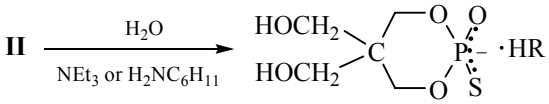


I **II**

The reaction was carried out at 120°C for 6 h with 88% yield. Thionophosphate **II** is a crystalline compound stable at prolonged storage. Note that previously [6, 7] the oxidation with sulfur of such bicyclophosphite on the basis of metriol was carried out for 5 min at 140°C with 89% yield. These data suggest that the frame system of **I** is rather conservative.

New phosphocyclic substance **II** was studied by TLC and ^{31}P, ^{1}H, ^{13}C NMR,[1] the NMR spectra were analyzed using the data of [8]. The ^{31}P NMR spectrum of compound **I** includes a singlet signal with δ_P 57.96 ppm, which is typical of this type of frame systems [3, 9]. ^{1}H NMR spectrum of the phosphocyclane **II** includes a pronounced singlet signal of the methylene protons of CH_2OH group and a doublet signal of methylene protons of CH_2O group in the bicyclic fragment of the molecule with a spin-spin coupling constants $^{3}J_{HP}$ 7.15 Hz. The assignment of the signals was performed with the use of a two-dimensional heteronuclear correlation spectroscopy (^{1}H–^{13}C HETCOR).

The resulting thionophosphonic derivative **II** was hydrolyzed in the presence of an organic base, triethylamine or cyclohexylamine (20-fold excess), at 140°C over 10–20 h. After the reaction completion, the products **III** and **IV** were obtained as ammonium salts, their yield reached 75%.



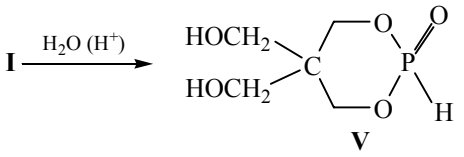
III, IV

R = $^{+}NEt_3$ (**III**), $^{+}NH_2C_6H_{11}$ (**IV**).

In the ^{31}P NMR spectra of the salts **III**, **IV** instead of the signal with δ_P 58 ppm of the original framework compound **II** the signals were observed characteristic of alkylenethionphosphates with δ_P 54 ppm. In the ^{1}H NMR spectra of compounds **III**, **IV** the main signals of the protons of the skeleton remained and the signals characteristic of the protons of the ammonium groups

[1] The same methods were used to prove the homogeneity and the structure of other substances obtained in this work.

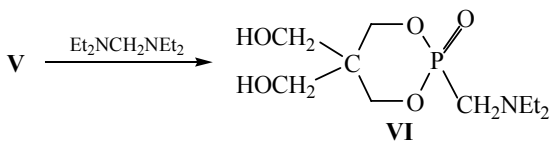
appeared. In the case of salt **III** it was a triplet (δ 1.14 ppm) and a quadruplet (δ 2.95 ppm) of the methyl and methylene protons of triethylammonium groups, and in the case of salt **IV,** the multiple signals (δ 0.99–2.03 ppm) of axial and equatorial methylene protons and a multiplet (δ 3.06 ppm) of the methine proton of the cyclohexyl fragment of the molecule. The low-field signals with δ 6.88–7.50 ppm in the spectra of compounds **III**, **IV** belonged to the protons of hydroxy groups. It should be noted that the chemical shift of the methine proton in the cyclohexane fragment of compound **IV** indicates that it occupies equatorial position in accordance with published data [10]. We also studied the acid hydrolysis of compound **I**.



V

The reaction of bicycle **I** with acidified water (pH 5) in dioxane proceeded over 20 h at 100–110°C. The hydrolysis of phosphite **I** led to opening of the framework fragment of the molecule and the formation of dimethylol hydrophosphoryl compound **V**. The desired product was isolated by precipitation from dioxane solution into hexane. The yield of chromatographically pure acid phosphite was 55%. ^{31}P NMR spectrum of the hydrophosphoryl compound contains a signal at δ_P 3.81 ppm, $^1J_{HP}$ 676.32 Hz. In the ^{1}H NMR spectrum of the hydophosphoryl compound there are characteristic signals of all proton groups. The proton signals of the hydrophosphoryl fragments appear as a doublet at δ 7.60 ppm split due to spin-spin coupling with the phosphorus nucleus, $^1J_{HP}$ 631 Hz. The signals of the protons of 1,3-dioxane functions are observed for the equatorial and axial protons as a multiplets at δ 4.42 and 4.75 ppm respectively. In addition, in the spectrum the signals are detected of methylene protons of two methylol groups at δ 4.07 and 4.17 ppm.

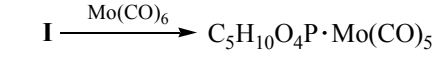
The hydrophosphite **V** was used for obtaining the aminomethylenephosphonate **VI** of a new type.



VI

In the ^{31}P NMR spectrum of **VI** there is a singlet signal δ_P 23.14 ppm.. In the ^{1}H NMR spectrum of compound **VI** the proton signals of the basic backbone of the molecule remained and the signals of the protons of N-ethyl group appeared as a triplet and quadruplet at δ 0.92 and 2.62 ppm, respectively. In addition, the spectrum contains a doublet signal of the PCH_2N group, $^2J_{HP}$ 10.65 Hz. The assignment of the signals is performed using two-dimensional heteronuclear correlation spectroscopy (^{1}H–^{13}C HETCOR).

We used an opportunity of obtaining a complex compound of molybdenum on the basis of bicyclephosphite **I**. Such complexes have not been obtained previously [9]. We found that compound **I** easily enters into the ligand exchange reaction with, for example, molybdenum hexacarbonyl, to form molybdenum compound **VII**.

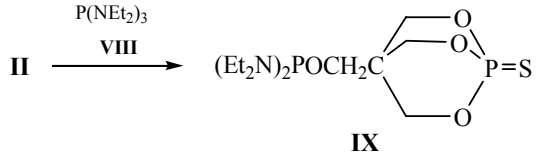


VII

The process of decarboxylation was carried out at a ligand–metal carbonyl molar ratio 1:1, in dioxane under argon atmosphere at 120°C for 1h.

The molybdenum complex **VII** was isolated from the dioxane solution by precipitation into hexane, yield 83%. Complex **VII** is a white powder, stable at the storage in an inert atmosphere for a long time. In the ^{31}P NMR spectrum of the pentaerythritol derivative **VII** there is a signal with δ_P 140.73 ppm. Note that the phosphorus chemical shifts of known molybdenum complexes based on di- and tripentaerythritol bisbicyclophosphites are similar: δ_P 138.96 [3] and 139.18 ppm [4], respectively. The ^{1}H NMR spectrum of complex **VII** contains all the signals characteristic of the ligand **I**. Thus, at the complex formation the structure of bicyclophosphite **I** was not destroyed. The composition and structure of molybdenum compound **VII** was also confirmed by MALDI TOF spectrum.

The next phase of the work consisted in the study of reactions of the free hydroxy group of the framework thionophosphate **II**. The work started with an equimolar phosphorylation of compound **II** with phosphoric hexaethyltriamide (**VIII**). In this way diamidophosphite **IX** was obtained.

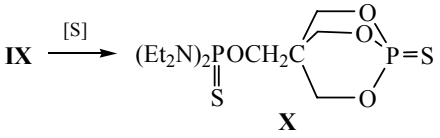


IX

The reaction with acyclic amidophosphite **VIII** was performed in a solution of anhydrous dioxane at room temperature within 10 h without removing the diethylamine liberated in the reaction. In the ^{31}P NMR

spectrum of crude phosphite **IX** two singlet signals were observed with a ratio of integral intensities 1:1, δ_P 57.9 ppm, belonging to phosphobicycle, and δ_P 136.6 ppm, related to the phosphorus atom in the acyclic part of the amidophosphite molecule.

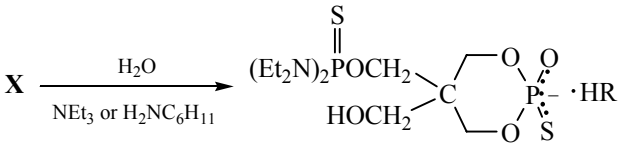
Phosphite **IX** was transformed without isolation into the corresponding dithionphosphate **X** (60°C, 5 h).



X

In the ^{31}P NMR spectrum of **X** two singlet signals were observed, related to acyclic and cyclic phosphorus atoms, δ_P 57.43 and 81.27 ppm, respectively, at a ratio of 1:1. In the ^{1}H NMR spectrum, besides the main signals of bicyclic fragment, the resonance of the protons of N-ethyl groups as characteristic triplet and multiplet in the δ areas of 1.11 and 3.05 ppm and a doublet of methylene protons of $POCH_2$ group with $^3J_{HP}$ 6.9 Hz were detected.

The framework compound **X** with the hydroxyl protected by amidothionophosphate function was subjected to alkaline hydrolysis in the presence of a nitrogen base, triethylamine or cyclohexylamine, under the conditions of hydrolysis of compound **II**, as described above.

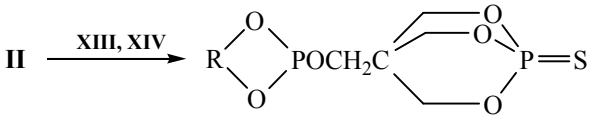


XI, XII

R = $^+NEt_3$ (**XI**), $^+NH_2C_6H_{11}$ (**XII**).

Target products **XI, XII** were isolated as ammonium salts with a yield of 85%. The salts **XI, XII** are oily substances stable at the storage. In their NMR spectra, along with ^{31}P signals in the region of δ_P 80 ppm belonging to the cyclic fragment, a singlet signal was observed in 1:1 ratio, with δ_P 54 ppm, characteristic of alkylenephosphates. In the ^{1}H NMR spectra of compounds **XI, XII** besides the signal of the main frame of the molecules, the proton signals of ammonium groups appeared, as in the case of salts **III**, **IV**. In the case of salt **XII** the methine proton of cyclohexyl fragment, as in the case of salt **IV**, occupies equatorial position (δ 3.05 ppm).

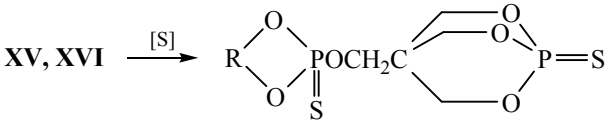
In the final stage of this section we studied phosphorylation of the free hydroxyl of phosphobicycle **II** using available phosphorylating means, namely, alkylenechlorophosphites **XIII, XIV,** at 0°C in a dioxane solution.



XV, XVI

R =  (**XIII, XV**),  (**XIV, XVI**).

Formation of alkylenephosphites **XV, XVI** was monitored by ^{31}P NMR spectroscopy: δ_P 58 and 138 ppm for compound **XV**, 58 and 123 ppm for compound **XVI**, at a ratio of integral intensities 1:1. Then the alkylenephosphites **XV, XVI** obtained were transformed without isolation into the corresponding thionophosphates **XVII, XVIII**. The sulfurization was carried out for 3–5 h at 60–70°C in dioxane. Note that the previously studied reactions [11] of pentaerythritol phosphorylation with chloroalkylenophosphites did not result in obtaining relevant pentaerythritol alkylenethionophosphates.



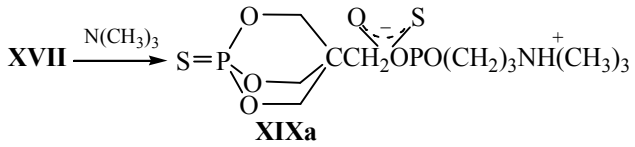
XVII, XVIII

Alkylenethionophosphates **XVII, XVIII** are crystalline compounds, stable for a long time when stored in an inert atmosphere. The ^{31}P NMR spectra of compounds **XVII, XVIII** contain singlets with δ_P 58.28 and 63.00 ppm, 57.16 and 61.55 ppm. respectively. In the ^{1}H NMR spectra of alkylenethionophosphates **XVII, XVIII** there are the signals of all protons, thus they confirm the structure of the substances obtained. Besides the signals of methylene protons of bicyclic fragment, the resonance of the protons of CH_2OR group as a doublet at δ 4.15–4.20 ppm with characteristic coupling constants with phosphorus atom were observed. In addition, in the spectrum of trimethylenethionophosphate **XVII** the signals of axial and equatorial protons of the phosphorylated ring were observed as typical multiplets at δ 1.61, 2.03, and 4.30 ppm. In the spectrum of dithionophosphate **XVIII** the signals of axial and equatorial protons of the phosphorylated ring have chemical shifts δ 3.92 and 4.11 ppm, and there are two singlet signals at δ 0.66 and 1.05 ppm related to the protons of methyl groups.

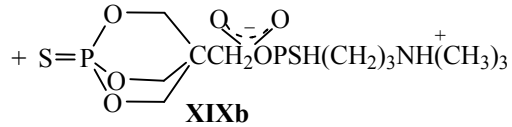
Propylenetionophosphate **XVII** was used for preparing from it original choline phosphoamphiphiles

XIXa and **XIXb**, which contain in their structure, along with phosphobicyclic fragment, the phosphocholine function.

The synthesis of this phospholipid was carried out by alkylation of trimethylamine with compound **XV** at 100–115°C for 5 h. The yield of target products **XIXa** and **XIXb** was 65%.



XIXa



XIXb

In the ^{31}P NMR spectrum of the reaction mixture besides the signal at δ_P 56.04 ppm belonging to the thion form of the phosphobetain **XIXa** a signal was observed in the region of δ_P 12.96 ppm, characteristic of tiolophosphate **XIXb** (the integral intensities ratio 1:1). The formation of tiolophosphate **XIXb** indicates that in the reaction thion–thiol isomerization occurs [12, 13]. We failed to isolate individual thiono- (**XIXa**) and tiolophosphates (**XIXb**).

In the ^{1}H NMR spectrum of a mixture of compounds **XIXa** and **XIXb** the main signals of the protons of the molecule backbone were retained, and the signals of the methyl protons of ammonium groups appeared (δ 3.25 ppm). An important characteristic of the spectrum of the mixture of compounds is the chemical shift of α-methylene protons of the phosphothiol fragment (δ 2.82 ppm) of betaine **XIXb**.

It is essential that the reaction of binuclear system **XV** with a nucleophilic reagent proceeds selectively at the mono-ring and does not affect the bulky fragment of the system.

EXPERIMENTAL

^{1}H, ^{13}C, and ^{31} P NMR spectra were obtained on a JEOL ECX-400 (400 MHz) instrument, chemical shifts for ^{1}H and ^{13}C are relative to TMS, for ^{31} P, to 85% phosphoric acid. Assignment of proton signals was carried out on the basis of double resonance and 2D heteronuclear correlation spectroscopy (HETCOR ^{1}H –^{13}C).

Mass spectral studies were performed on a Bruker Ultra Flex instrument with a time-of-flight detector (TOF) by the method of a matrix-assisted laser desorption and ionization (MALDI) (l 337 nm) using trihydroxyanthracene as a template.

For elemental analysis a Perkin-Elmer 2400 Analyzer was used.

All syntheses involving compounds of trivalent phosphrus were performed in a dry argon atmosphere. Adsorption chromatography was performed on a column of 10 mm diameter packed with L 100–250 μm silica gel; R_f values were identified by TLC on Silufol UV-254 plates using systems of ethyl acetate–acetonitrile, 2:1 (A), benzene–ethyl acetate–acetonitrile, 3:1:1 (B), chloroform–methanol, 3:1 (C) methanol–water, 3:1 (D), hexane–dioxane, 3:1 (E), benzene–dioxane, 1:2 (F), benzene–dioxane, 3:1 (G).

Melting points were determined in sealed capillaries, heating rate of 1 deg min^{-1}.

Phosporic hexaethyltriamide (**VIII**) was prepared by the method [14], 2-chloro-1,3,2-dioxaphos-phorinane (**XIII**) and 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane (**XIV**), according to techniques [15]. 1-Methyl-4-phospha-3,5,8-trioxabicyclo[2,2,2]octane (**I**) was synthesized by the method of [1] (mp 97–98°C). Constants of these compounds were consistent with the published data.

4-Hydroxymethyl-2,6,7-trioxa-1-phosphabicyclo-[2,2,2]octane-1-thionooxide (**II**). A solution of 0.2 g of bicyclophosphite (I) (δ_P 94.6 ppm) and 0.04 g of finely ground sulfur in 4 ml of anhydrous dioxane was heated at 120°C for 6 h. Excess sulfur was filtered off, dioxane was removed in a vacuum. To free the resulting reaction product **II** from traces of sulfur it was dissolved in acetone (2×3 ml) followed by filtration and distilling off the solvent. The residue was dried for 3 h (40°C, 1 mm Hg). Yield of compound **II** 0.21 g (88.2%), mp 150–152°C, R_f 0.30 (A), 0.10 (B), 0.50 (C). ^{1}H NMR spectrum (C_5D_5N), δ, ppm: 3.51 (2H, $C\underline{H}_2OH$), 4.71 q (8H, CH_2 OP, $^3J_{HP}$ 7.15 Hz), 6.70 br.s (1H, OH). ^{13}C NMR spectrum (C_5D_5N), δ_C, ppm: 38.99 d (>C<, $^3J_{CP}$ 3.47 Hz), 59.25 s (CH_2OH), 76.77 g (CH_2OP, $^2J_{CP}$ 7.70 Hz).^{31} P NMR spectrum (pyridine), δ_P, ppm: 57.96 s. Found, %: C 30.45, H 4.33, P 15.58. $C_5H_9O_4PS$. Calculated, %: C 30.61, H 4.62, P 15.79. *M* 196.

2-Hydrotriethylammonium-5,5-dioxymethyl-2-thio-1,3,2-dioxaphosphorinane (**III**). A solution of 0.1 g of bicyclothionophosphate **II**, 0.18 g of water, 1.03 g of triethylamine (molar ratio 1:20:20) in 10 ml of acetonitrile (pH > 10) was heated in a sealed tube at 140°C for 20 h. Acetonitrile, triethylamine, and water were removed in a vacuum and the remaining oily substance was dissolved in 2 ml of dioxane and reprecipitated with hexane (2×3 ml). Salt **III** was kept for 4 h at 80°C (1 mm Hg) Yield of compound **III** 0.1 g

(65.2%), n_D^{20} 1.4930, R_f 0.45 (C). ^{1}H NMR spectrum (C_5D_5N), δ, ppm: 1.14 m {9H, $[HN(CH_2C\underline{H}_3)_3]^+$, $^3J_{HH}$ 7.5 Hz}, 2.95 q {6H,$[HN(C\underline{H}_2CH_3)_3]^+$, $^3J_{HP}$ 11.95 Hz}, 3.95 s and 4.38 s (4H, $C\underline{H}_2OH$), 4.55 m ($2H_e$) and 5.15 m ($2H_a$) (OCH_2CCH_2OR, $^2J_{HaHe}$ 10.6 Hz,, $^3J_{HP}$ 5.84 Hz,), 8.10 br.s (3H, NH, OH). ^{13}C NMR spectrum (C_5D_5N), δ_C, ppm: 8.45 $[HN(CH_2\underline{C}H_3)_3]^+$, 42.83 s (>C<, $^3J_{CP}$ 3.9 Hz), 45.71 d {$[HN(\underline{C}H_2CH_3)_3]^+$, $^2J_{CP}$ 4.95 Hz}, 60.79 and 61.99 (CH_2OH), 69.32 d ($O\underline{C}H_2C\underline{C}H_2OR$, $^2J_{CP}$ 3.08 Hz). ^{31}P NMR spectrum (pyridine), δ_P 53.89 ppm. Found, %: C 42.05, H 8.48, P 10.03. $C_{11}H_{26}NO_5PS$. Calculated, %: C 41.89, H 8.31, P 9.82. *M* 315.

2-Hydrocyclohexylammonium-5,5-dioxymethyl-2-thio-1,3,2-dioxaphosphorinane (**IV**) was obtained similar to salt **III** from 0.05 g of bicycle **II**, 0.09 g of water, and 0.5 g of cyclohexylamine (molar ratio 1:20:20) in 3 ml of acetonitrile (pH > 10) at 140°C for 10 h. Then, acetonitrile, cyclohexylamine, and water were removed in a vacuum and the residue was washed with hexane (2×2 ml). Salt **IV** was kept for 4 h at 80°C (1 mm Hg). Yield 0.06 g (75%) n_D^{20} 1.5760, R_f 0.33 (B). ^{1}H NMR spectrum (C_5D_5N), δ, ppm: 0.99 m [$1H_e$, $NCH(CH_2CH_2)_2C\underline{H}_2$], 1.11 m [$2H_e$, $NCH(CH_2C\underline{H}_2)_2CH_2$], 1.15 m [$2H_e$, $NCH(C\underline{H}_2CH_2)_2CH_2$], 1.34 m [$1H_a$, $NCH(CH_2CH_2)_2C\underline{H}_2$, $^2J_{HaHe}$ 9.73 Hz], 1.46 m [$2H_a$, $NCH(CH_2C\underline{H}_2)_2CH_2$, $^2J_{HaHe}$ 10.73 Hz], 2.03 m [$2H_a$, $NCH(C\underline{H}_2CH_2)_2CH_2$, $^2J_{HaHe}$ 11.3 Hz], 3.06 m (1H, $H_3N^+C\underline{H}$), 3.95 br.s (4H, $C\underline{H}_2OH$), 4.57 m ($2H_e$) and 4.72 m ($2H_a$) (OCH_2CCH_2OR, $^2J_{HaHe}$ 11.5 Hz, $^3J_{HP}$ 6.40 Hz), 6.88–7.50 br.s (5H, OH, H_3N^+). ^{13}C NMR spectrum (C_5D_5N), δ_C, ppm: 23.09 [$NCH(CH_2\underline{C}H_2)_2CH_2$], 25.70 [$NCH(\underline{C}H_2CH_2)_2CH_2$], 33.26 [$NCH\ (CH_2\ CH_2)_2\underline{C}H_2$], 42.69 (1C, >C<), 48.39 (CH_2OH) 50.36 [$NCH(CH_2CH_2)_2CH_2$], 69.24 d ($O\underline{C}H_2C\underline{C}H_2OP$, $^2J_{CP}$ 10.54 Hz). ^{31}P NMR spectrum (pyridine), δ_P 54.80 ppm. Found, %: C 42.61, H 13.88, P 10.16. $C_{11}H_{24}NO_5PS$. Calculated, %: C 42.43, H 13.55, P 9.95. *M* 311.

2-Hydro-2-oxo-5,5-dioxymethyl-1,3,2-dioxaphosphorinane (**V**). A suspension of 0.2 g of bisbicyclophosphite **I** (δ_P 94.61 ppm) and 0.06 g of water (pH 5) (molar ratio 1:3) in 5 ml of anhydrous dioxane was heated in a sealed ampule for 20 h at 100–110°C. The solution was decanted and acidic phosphite **V** was precipitated by hexane and washed with the same solvent (2×2 ml). The desired product was kept for 3 h at 50°C (1 mm Hg). Yield 0.12 g (55%) 1.5039, R_f 0.85 (D). ^{1}H NMR spectrum (C_5D_5N), δ, ppm: 4.07 s and 4.17 s (4H, $C\underline{H}_2OH$), 4.42 m ($2H_e$) and 4.51 m, 4.75 m ($2H_a$) (CH_2OP), 7.60 d [1H, P(O)H, $^1J_{PH}$ 631 Hz]. ^{31}P NMR spectrum (dioxane), δ_P, ppm: 3.81 s, $^1J_{PH}$ 676.32 Hz. Found, %: C 33.12, H 6.31, P 17.25. $C_5H_{11}O_5P$. Calculated, %: C 32.97, H 06.09, P 17.01. *M* 182.

2-Diethylaminomethyl-2-oxo-5,5-dioxymethyl-1,3,2-dioxaphosphorinane (VI). 0.1 g of hydrophosphite **V** and 0.93 g of tetraethylmethylenediamine in 20 ml of dioxane was heated in a flask with a reflux condenser for 9 h at 110°C. Solvent and volatile reaction products were removed in a vacuum, the residual oil was washed with hexane (2×2 ml). The target phosphonate **VI** was kept for 3 h at 40°C (1 mm Hg). Yield of compound **VI** 0.1 g (68%), n_D^{20} 25, R_f 0.75 (C). ^{1}H NMR spectrum (C_5D_5N), δ, ppm: 0.92 t (6H, $NCH_2C\underline{H}_3$, $^3J_{HH}$ 7.2 Hz), 2.62 q (4H, $NC\underline{H}_2CH_3$, $^4J_{HP}$ 4.02 Hz), 2.92 br.d (2H, PCH_2N, $^2J_{HP}$ 10.65 Hz), 4.04 s and 4.14 s (4H, $C\underline{H}_2OH$), 4.76 br.m ($2H_e$) and 4.80 br.m ($2H_a$) (CCH_2OP, $^3J_{PH}$ 6.23 Hz). ^{13}C NMR spectrum (C_5D_5N), δ_C, ppm: 13.57 ($NCH_2\underline{C}H_3$), 29.76 (>C<), 46.77 d ($N\underline{C}H_2CH_3$, $^3J_{CP}$ 15.3 Hz), 63.27 d ($P\underline{C}H_2NCH_2CH_3$, $^1J_{CP}$ 11.58 Hz), 68.51 s and 69.51 s (CH_2OH), 76.92 d ($C\underline{C}H_2OP$, $^2J_{CP}$ 10.5 Hz). ^{31}P NMR spectrum (dioxane), δ_P 23.14 ppm. Found, %: C 45.24; H 8.57; P 11.83. $C_{10}H_{22}NO_5P$. Calculated, %: C 44.94; H 8.30; P 11.59. *M* 267.

1-Methyl-4-phospha-3,5,8-trioxabicyclo[2,2,2]-octane molibdenum complex (VII). An ampule with a solution of 0.09 g of bicyclophosphite **I** and 0.14 g of molibdenum hexacarbonyl (reagent ratio 1: 1) in 5 ml of dioxane was heated for 1 h at 120°C. The formed complex **VII** was precipitated from the reaction mixture with hexane. The solvents were decanted and the precipitate was washed with hexane (2×5 ml) and dried for 1 h at 50°C (1 mm Hg). Yield of the complex **VII** 0.18 g (83%), mp 243°C (decomp.), R_f 0.45 (C). ^{1}H NMR spectrum (C_5D_5N), δ, ppm: 3.35 br.s (2H, $C\underline{H}_2OH$), 4.43 br.d (6H, CH_2OP, $^3J_{HP}$ 1.83 Hz), 6.75 br.s (1H, $CH_2O\underline{H}$). ^{13}C NMR spectrum (C_5D_5N), δ_C, ppm: 37.76 (>C<), 60.79 ($\underline{C}H_2OH$), 72.71 d ($C\underline{C}H_2OP$, $^2J_{CP}$ 7.24 Hz), 207.30 d.d and 211.84 d.d (5CO, $^1J_{CP}$ 13.37 and 17.25 Hz). ^{31}P NMR spectrum (pyridine), δ_P 140.73 ppm. Found, %: C 30.25; H 2.84; P 7.98. $C_5H_{10}O_4P{\cdot}Mo(CO)_5$. Calculated, %: C 29.95; H 2.51; P 7.72. *M* 401. Mass spectrum, *m*/*e* (*I*, %), found 316.811 (100) [*M* – 3CO], calculated 316.965 [*M* – 3CO].

4-Diethylamidothionophosphatoxymethyl-2,6,7-trioxa-1-phosphabicyclo[2,2,2]octane-1-thionooxide (X). 0.15 g of bicyclic compound **II** and 0.19 g of phosphorous hexaethyltriamide **VIII** in 5 ml of anhydrous dioxane was stirred for 10 h at 25°C. The formation of diamidophosphite **IX** was monitored by

the method of ^{31}P NMR spectroscopy (dioxane), δ_P, ppm: 57.86 s and 136.69 s (integral intensity ratio 1:1). Then to the reaction mixtre was added 0.03 g of finely ground sulfur, and the mixture was kept at 60°C for 5 h. The sulfur excess was filtered off, and dioxane was removed in a vacuum. The diamidodithionophosphate **X** was purified by chromatography on a column packed with silica gel (5 g), filled with benzene. Compound **X** was eluted with 20 ml of a benzene–dioxane 1:2 mixture. The solvents were removed in a vacuum, the residue was kept for 3 h at 40°C (1 mm Hg). Yield of compound **X** 0.22 g (70 %), mp 83–84°C, R_f 0.35 (E), 0.55 (F). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.11 t (12H, $NCH_2C\underline{H}_3$, $^3J_{HH}$ 6.9 Hz), 3.05 m (8H, $NC\underline{H}_2CH_3$, $^3J_{HP}$ 12.4 Hz), 3.72 d (2H, $C\underline{H}_2OP$, $^3J_{HP}$ 6.9 Hz), 4.53 d (6H, CCH_2OP, $^3J_{PH}$ 6.8 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.19 ($NCH_2\underline{C}H_3$), 40.24 d ($N\underline{C}H_2CH_3$, $^2J_{CP}$ 5.8 Hz), 61.38 (>C<), 67.18 ($POCH_2$), 75.63 d ($POCH_2C$, $^2J_{CP}$ 7.7 Hz). ^{31}P NMR spectrum (chloroform), δ_P, ppm: 57.43 s and 81.27 s (integral intensity ratio 1:1). Found, %: C 39.01; H 7.28; P 15.51. $C_{13}H_{28}N_2O_4P_2S_2$. Calculated, %: C 38.80; H 7.01; P 15.39. *M* 402.

5-Diethylamidothionophosphatoxymethyl-5-oxymethyl-2-hydrotriethylammonium-2-thio-1,3,2-dioxyphosphorinane (XI) was synthesized similar to salt **III** from 0.1 g of diamide **X**, 0.09 g of water, and 0.50 g of triethylamine (mole ratio 1:20:20) in 5 ml of acetonitrile (pH > 10) at 130–140°C for 15 h. Then acetonitrile, triethylamine, and water were removed in a vacuum, the residue was washed with hexane (2× 3 ml). Salt **XI** was kept for 3 h at 80°C (1 mm Hg). Yield 0.1 g (80%), n_D^{20} 1.5440, R_f 0.49 (C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.03 t (12H, $NCH_2C\underline{H}_3$, $^3J_{HH}$ 6.9 Hz), 1.29 t {9H, $[HN(CH_2C\underline{H}_3)_3]^+$, $^3J_{HH}$ 7.20 Hz}, 3.04 q {6H, $[HN(C\underline{H}_2CH_3)_3]^+$, $^3J_{HP}$ 13.8 Hz}, 3.08 q (8H, $NC\underline{H}_2CH_3$, $^3J_{HP}$ 12.2 Hz), 3.35 br.s (2H, $C\underline{H}_2OH$), 3.95 m (2H$_e$) and 4.30 m (2H$_a$) [OCH_2CCH_2O, $^2J(H_aH_e)$ 11.31 Hz, $^3J_{HP}$ 4.7 Hz], 4.17 d (2H, $POCH_2$, $^3J_{HP}$ 9.87 Hz), 5.74 br.s (1H, HN^+), 6.34 br.s (1H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 8.72 $[HN(CH_2\underline{C}H_3)_3]^+$, 14.49 d ($NCH_2\underline{C}H_3$, $^3J_{CP}$ 3.75 Hz), 39.62 $[HN(C\underline{H}_2CH_3)_3]^+$, 45.82 d ($N\underline{C}H_2CH_3$, $^2J_{CP}$ 5.82 Hz), 60.81 (>C<), 62.05 d ($POCH_2$, $^2J_{CP}$ 4.01 Hz), 68.84 d ($PO\underline{C}H_2C$, $^2J_{CP}$ 5.86 Hz). ^{31}P NMR spectrum (chloroform), δ_P, ppm: 54.16 s and 79.93 s (integral intensity ratio 1:1). Found, %: C 43.91; H 8.93; P 12.01. $C_{19}H_{45}N_3O_5P_2S_3$. Calculated, %: C 43.74; H 8.69; P 11.88. *M* 522.

5-Diethylamidothionophosphatoxymethyl-5-hydroxymethyl-2-hydrocyclohexylammonium-2-thio-1,3,2-dioxaphosphorinane (XII) was synthesized analogous to salt **IV** from 0.13 g of diamide **X**, 0.12 g of water, and 1.1 g of cyclohexylamine (mole ratio 1:20:20) in 8 ml of acetonitrile (pH > 10) at 140°C over 8 h. Then acetonitrile, cyclohexylamine, and water were removed in a vacuum, and the residue was washed with hexane (2×3 ml). Salt **XII** was kept for 3 h at 80°c (1 mm Hg). Yield 0.14 g (85%), n_D^{20} 1.5870, R_f 0.35 (C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.05 t (12H, $NCH_2C\underline{H}_3$, $^3J_{HH}$ 7.1 Hz), 1.08 m [1H$_e$, $NCH(CH_2CH_2)_2C\underline{H}_2$], 1.19 m [2H$_e$, $NCH\cdot(C\underline{H}_2CH_2)_2CH_2$], 1.28 m [1H$_e$, $NCH(CH_2C\underline{H}_2)_2CH_2$], 1.55 m [1H$_a$, $NCH(CH_2CH_2)_2C\underline{H}_2$, $^2J(H_aH_e)$ 11.63 Hz], 1.69 m [2H$_a$, $NCH(CH_2C\underline{H}_2)_2CH_2$, $^2J(H_aH_e)$ 12.32 Hz], 1.98 m [2H$_a$, $NCH(C\underline{H}_2CH_2)_2CH_2$, $^2J(H_aH_e)$ 11.03 Hz], 3.05 m (1H, $H_3N^+C\underline{H}$), 3.06 (8H, $NC\underline{H}_2CH_3$, $^3J_{HP}$ 12.53 Hz), 3.37 br.s (2H, $C\underline{H}_2OH$), 3.91 m (2H$_e$) and 4.27 m (2H$_a$) [OCH_2CCH_2OP, $^2J(H_aH_e)$ 11.56 Hz, $^3J_{HP}$ 4.86 Hz], 4.13 d (2H, CH_2OPN, $^3J_{HP}$ 8.89 Hz), 5.98 br.s (4H, OH, H_3N^+). ^{13}C NMR spectrum (C_5D_5N), δ_C, ppm: 14.49 ($NCH_2\underline{C}H_3$), 24.94 $[NCH(CH_2\underline{C}H_2)_2CH_2]$, 25.07 $[NCH(\underline{C}H_2CH_2)_2CH_2]$, 32.34 $[NCH(CH_2CH_2)_2\underline{C}H_2]$, 40.19 d ($N\underline{C}H_2CH_3$, $^2J_{CP}$ 3.87 Hz), 40.39 (>C<), 50.69 $[N\underline{C}H(CH_2CH_2)_2CH_2]$, 60.05 ($CH_2OH$), 60.08 br.d ($POCH_2C$, $^2J_{CP}$ 4.00 Hz), 68.80 d ($O\underline{C}H_2C\underline{C}H_2OP$, $^2J_{CP}$ 5.66 Hz). ^{31}P NMR spectrum (chloroform), δ_P, ppm: 54.32 and 80.57 (integral intensity ratio 1:1). Found, %: C 44.13; H 8.61; P 12.21. $C_{19}H_{43}N_3O_5P_2S_2$. Calculated, %: C 43.91; H 8.34; P 11.92. *M* 520.

1,3-Propylenethionophosphate-4-oxymethyl-2,6,7-trioxa-1-phosphabicyclo[2,2,2]octane-1-thionooxide (XVII). To a solution of 0.14 g of 2-chloro-1,3,2-dioxaphosphorinane **XIII** in 5 ml of the water-free dioxane at stirring and cooling to 0°C was added dropwise a mixture of 0.2 g of bicyclophosphite **II** and 0.1 g of triethylamine in 5 ml of the same solvent. The reaction mixture was kept at this temperature for 0.5 h, and then the temperature was raised in 0.5 h to the room temperature. The formation of propylenephosphite **XV** was monitored by ^{31}P NMR spectroscopy (dioxane), δ_P, ppm: 57.64 s and 138.48 s (integral intensity ratio 1:1). Pyridine hydrochloride was filtered off, and to the filtrate was added 0.04 g of finely ground sulfur, then temperature was raised to 60°C, and the reaction mixture was kept at this temperature for 3 h. The sulfur excess was filtered off, dioxane was removed in a vacuum. To remove the sulfur traces reaction product **XVII** obtained was dissolved in acetone (2×3 ml) followed by filtrartion and distilling the solvent off. The propylenedithionophosphate **XVII** was purified additionally by chromatography on a

column with silica gel (5 g) filled with benzene. Compound **XVII** was eluted with 10 ml of a benzene–dioxane 2:1 mixture. The solvents were removed in a vacuum, the residue was kept for 2 h at 40°C (1 mm Hg). Yield of compound **XVII** 0.25 g (75%), mp. 203–205°C, R_f 0.49 (G), 0.00 (E). ^{1}H NMR spectrum (C_5D_5N), δ, ppm: 1.61 m (1H$_e$) and 2.03 m (1H$_a$) ($OCH_2C\underline{H}_2CH_2O$), 4.15 d (2H, CCH_2OP, $^3J_{PH}$ 11.99 Hz), 4.30 br.m (4H, $OC\underline{H}_2CH_2C\underline{H}_2O$), 4.79 d (6H, $POCH_2C$, $^2J_{PH}$ 6.9 Hz). ^{13}C NMR spectrum (C_5D_5N), δ_C, ppm: 26.14 d ($OCH_2\underline{C}H_2CH_2O$, $^2J_{PC}$ 7.6 Hz), 37.62 d.d (>C<, $^3J_{PC}$ 3.8 Hz), 64.26 d ($C\underline{C}H_2OP$, $^2J_{PC}$ 6.95 Hz), 69.10 d ($O\underline{C}H_2CH_2\underline{C}H_2O$, $^2J_{PC}$ 7.7 Hz), 75.69 d ($PO\underline{C}H_2$, $^2J_{PC}$ 7.6 Hz). ^{31}P NMR spectrum (pyridine), δ_P, ppm: 58.28 s and 63.00 s (integral intensity ratio 1:1). Found, %: C 29.23; H 4.56; P 18.93. $C_8H_{14}O_6\cdot P_2S_2$. Calculated, %: C 28.92; H 4.25; P 18.64. *M* 332.

1,3-(5,5-Dimethyl)propylenethionophosphate-4-oxymethyl-2,6,7-trioxa-1-phosphabicyclo[2,2,2]-octane-1-thionoxide (XVIII) was synthesized by analogy with compound **XVII** from 0.21 g of 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane **XIV**, 0.25 g of **II**, 0.13 g of triethylamine, and 0.05 g of sulfur in 8 ml of anhydrous dioxane (5 h, 80°C). Phosphite **XVI** formation was monitored by ^{31}P.NMR spectroscopy (dioxane), δ_P, ppm: 57.27 s and 122.95 s (integral intensity ratio 1:1). Dithionophosphate **XVIII** was purified by chromatography on a column with silica gel (10 g) filled with benzene, eluent 25 ml of a benzene–dioxane 3:1 mixture. The solvents were re-moved in a vacuum, and the precipitate was kept for 2 h at 40°C (1 mm Hg). Yield 0.37 g (80%), mp 230–232°C, R_f 0.50 (G), 0.1 (E). ^{1}H NMR spectrum (C_5D_5N), δ, ppm: 0.66 br.s and 1.05 br.s [6H, $OCH_2C\cdot(C\underline{H}_3)_2CH_2O$], 3.92 m (2H$_e$) and 4.11 m (2H$_a$) [$OC\underline{H}_2C\cdot(CH_3)_2C\underline{H}_2O$, ^2J (H$_aH_e$) 11.09 Hz, $^3J_{HP}$ 3.64 Hz], 4.20 br.d (2H, CH_2OP, $^3J_{PH}$ 7.09 Hz), 4.79 br.d (6H, CCH_2OP, $^3J_{PH}$ 6.75 Hz).^{13}C NMR spectrum (C_5D_5N), δ_C, ppm: 14.21 (>C<), 20.12 [$OCH_2C(C\underline{H}_3)CH_2O$], 37.62 d.d (>C<, $^3J_{PC}$ 4.02 Hz), 64.66 d ($C\underline{C}H_2OP$, $^2J_{PC}$ 3.46 Hz), 75.68 d ($PO\underline{C}H_2$, $^2J_{PC}$ 7.6 Hz), 77.80 d [2C, $O\underline{C}H_2C(CH_3)\cdot\underline{C}H_2O$, $^2J_{PC}$ 7.6 Hz]. ^{31}P NMR spectrum (pyridine), δ_P, ppm: 57.16 s and 61.55 s (integral intensity ratio 1:1). Found, %: C 33.61; H 5.24; P 17.36. $C_{10}H_{18}O_6P_2S_2$. Calculated, %: C 33.33; H 5.03; P 17.19. *M* 360.

***O,O'*-Thionophosphohomocholine-4-oxymethyl-2,6,7-trioxa-1-phosphabicyclo[2,2,2]octane-1-thionooxide (XIXa) and *O,S*-thiolophosphohomocholine-4-oxymethyl-2,6,7-trioxa-1-phosphabicyclo[2,2,2]-octane-1-thionooxide (XIXb).** A sealed ampule with a solution of 0.15 g of dithionophosphate **XVII** and 0.09 g of trimethylamine in 20 ml of anhydrous acetonitrile was kept for 5 h at 100–115°C. The solvents were removed in a vacuum, the oily residue was washed consecutively with benzene (2×5 ml) and hexane (2×5 ml), and dried for 2 h at 40°C (1 mm Hg). The mixture of homocholines **XIXa** and **XIXb,** yield 0.1 g (65%), mp 238–241°C (wetting at 135°C), R_f 0.00 (G), 0.52 (D). ^{1}H NMR spectrum ($CDCl_3$– CD_3OD, 99:1), δ, ppm: 1.15 br.m (2H, $POCH_2\cdot C\underline{H}_2CH_2N^+$), 2.82 br.m (2H, $PSC\underline{H}_2CH_2CH_2N^+$, $^3J_{PH}$ 5.48 Hz), 3.25 br.s [9H, $N^+(CH_3)_3$], 3.55 br.m (2H, CH_2N^+), 3.65 br.m (2H, $POC\underline{H}_2CH_2CH_2N^+$), 3.95 d (2H, CH_2OP, $^3J_{PH}$ 13.81 Hz), 4.55 d (6H, OCH_2O, $^3J_{PH}$ 6.69 Hz). ^{31}P NMR spectrum (chloroform–methanol, 99:1), δ_P, ppm: 12.96 br.s **XIXb** and 56.04 br.s **XIXa,** integral intensity ratio 1:1. Found, %: C 35.38; H 6.31; P 16.72. $C_{11}H_{23}NO_5\cdot P_2S_2$. Calculated, %: C 35.19; H 6.18; P 16.50. *M* 375.

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