ISSN 1070-3632, Russian Journal of General Chemistry, 2006, Vol. 76, No. 7, pp. 1048–1054. © Pleiades Publishing, Inc., 2006.
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Dipentaerethrite in the Synthesis of Model Amidophosphate Phospholipids

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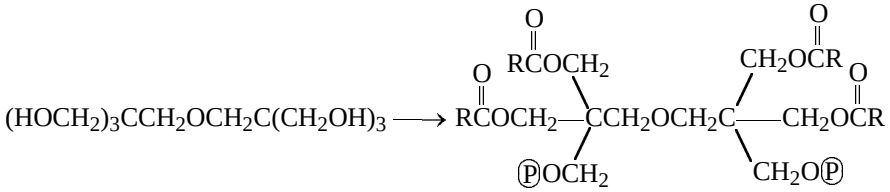
Received November 25, 2005

Abstract — A productive method for the synthesis of original phospholipid architectures is developed based on the available reagent dipentaerythritol. Introduction of the phosphoric function to the system is achieved by using phosphoric hexaethyltriamide.

DOI: 10.1134/S1070363206070073

Traditional studies in the chemistry of phosphoglycerols, phosphoingosides and other well studied natural phospholipids in the recent years were supplimented with reports on the synthetic systems with complicated oligohydroxyl and other oligofunctionalized nuclei in their base [1–8]. Our publication is denoted to this new scientific area, namely, to the development of design of original phospholipids, the derivatives of the available hexaol dipentaerythritol (**I**). This publication continues our earlier study of new phospholipids of non-glycerol type using trivalent phosphorus compounds [9–11].

The main purpose of our investigation is further development of synthetic approach to the phospholipid architectures **II** which include dipentaerytritol bone framed by two phosphoric and four carboxylic groups arranged symmetrically relatively to central ether oxygen atom.



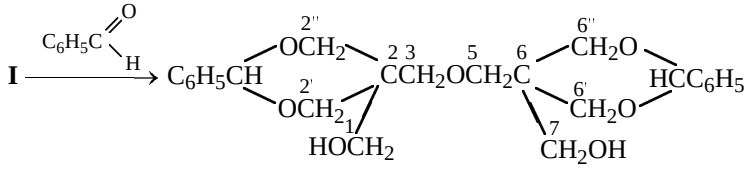
(1)

I **II**

To achieve this purpose we split modification of the hexaol **I** into the following steps:

(1) Finding ability of introducing symmetrically two protecting groups blocking four hydroxyls in the parent polyol. (2) Symmetrical introducing of two reactive residues of diamidophosphoric acid to the obtained compound. (3) Stabilizing the introduced atoms of trivalent phosphorus by oxidation. (4) Complete deleting of two protecting groups and liberation of four hydroxyls. (5) Complete or incomplete acylating of the free hydroxyls. Actually, each the step appeared to be a nontrivial challenge and required finding optimal reagents and the process conditions.

For blocking two hydroxyl pairs in each pentaerythritol part of compound **I** we used the method of acetalization [12–15]. The best result was obtained in reaction of hexaol **I** with benzaldehyde.



(2)

III

Preparation of the diacetal **III** in a suspension of hexaol **I** with benzaldehyde in boiling benzene [16, 17] or toluene [17] using a Dean–Stark trap and *p*-toluenesulfonic acid monohydrate as a catalyst has been described. The authors proposed a complicated and continuous procedure for the acetalization.

Regardless the published data [16, 17] we used for the dual bezylation of hexaol **I** the methods based on the catalysis by hydrochloric or phosphorotungstic acids, which allowed to simplify the pricess of preparation of compound **III** considerably. The diacetal **III** yields achieve 90%. We tested several methods of conducting the synthesis and isolation of the target compound **III**. One of the method consisted of reaction without a solvent (method 1) under flow of argon at 90–95°C for 3 h in a vacuum 100 mm Hg in the presence of a few drops of concentrated hydrochloric acid (the same temperature conditions, argon atmosphere and catalysis by hydrochloric acid were applied in the procedures of the diacetal **III** synhesis 1 to 4 and catalysis by phosphortungstic acid in 5).

The target compound **III** was isolated by column chromatography (procedure *a*). Yield of chromatographically pure diacetal **III** achieved 49%. As an adsorbent, we used aluminum oxide or silica gel. We found that the type of carrier practically does not affect yield of the final compound **III**. Increase 2–3-fold in amount of catalyst also has no effect on the yield.

This method of preparation of the diacetal **III** (method *1*) shows a few disadvantagues in the preparative aspects. The main one is heterogenous medium of the reaction. A part of the parent compound **I** (ca. 10%) does not enter the reaction with benzaldehyde and remains unchanged to the end of the process.

To provide homogeneity to the reaction mixture of the hexaol **I** and benzaldehyde we performed experiments using dimethylformamide (DMF) as a reaction medium (method *2*). However in this case also the homogeneity is achieved only in time, after 1 to 1.5 h of beginning the process, despite a significant amount of DMF. The target copound **III** was isolated by chromatography in 50% yield (procedure *a*).

Another procedure for the isolation of diacetal **III** in the synthesis by the method *2* consists in the mixing the reaction mixture with 1% aqueous potassium carbonate. The target compound **III** dropped from the solution as a fine disperse precipitate which then was filtered off (procedure *b*). Yield of **III** achieved 71%.

As a solvent for benzylidenation of hexaol **I**, we tested dimethylsulfoxide (DMSO) (method *3*). For isolation we used procedure *b* and obtained **III** in 61% yield.

Finally we found better to prepare **III** using DMF–DMSO mixture in the ratio 1 : 2 by volume (method *4*). Yield of the product **III** by procedure *b* achieves 90%.

As a catalyst in the synthesis of diacetal **III** we also used phosphorotungstic acid (method *5*). Reaction was performed in 1 : 2 DMF–DMSO mixture. This method is useful for preparative purpose due to good solubility of the heteropolyacid in this solvent mixture. Isolation according to procedure b yielded 75% of **III**.

Additional purification of diacetal **III** after isolation by *a* or *b* procedure can be achieved by its dissolving in chloroform followed by precipitation with hexane or by recrystallization from 1 : 3 benzene–dioxane mixture or from isopropyl alcohol. Yield after purification achieved 80–90%.

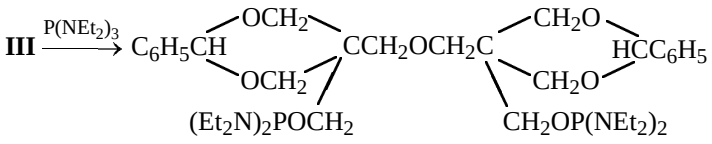
The diacetal **III** was isolated as a mixture of three configurational isomers: *cis*-*cis*, *cis*-*trans*, and *trans*-*trans*. The geometric isomers are defined as *cis*-1,3 or *trans*-1,3 isomers of dioxane in correspondence with the position of phenyl and H substituted hydroxymethyl groups relatively to the ring, taking into account the publication [17].

The ^{1}H NMR spectrum of diacetal **III** contains signals of the protons of hydroxyl groups (δ 2.36 ppm), doublets of methylene protons and a broad singlet of methine protons in 1,3-dioxolane ring (δ 3.78, 4.10, and 5.42 ppm respectively), a dobulet of the protons of methylene groups possessing hydroxyl (δ 3.84 ppm), and the signals of other protons in this structure (see the Experimental).

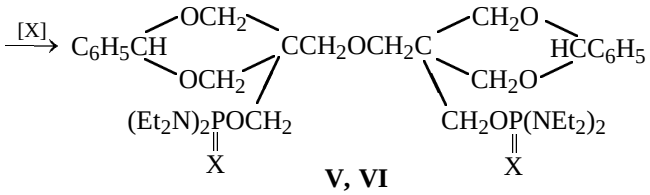
We used successfully the diol **III** bisacetal for preparation on this basis of tetraamonodiphosphate phospholipids. The diol **III** by reaction with phosphorous hexaethyltriamide was transformed to the amidophosphite **IV** used as a parent compound for preparation of phosphochalcogen derivatives **V** and **VI**.

Phosphorylation was performed with anhydrous dioxane as a solvent at room temperature (25°C) without removing the diethylamine formed in the reaction. In the ^{31}P NMR spectrum of the crude amidophosphite **IV** was observed a broad singlet at δ_P 135 ppm typical of diamidophosphites. Compound **IV** was used in further syntheses without additional purification.

We found that bisdiamidophosphite **IV** can be widely used in the synthesis. It readily adds sulfur or selenium to form thiono- (**V**) and seleno-phosphates (**VI**), respectively.



IV

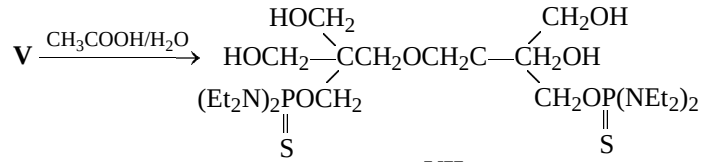


V, VI (3)

Note that this reaction proceeds readily at room temperature. Yields of the phosphochalcogenic products **V** and **VI** isolated by chromatography achieved 72% over two steps. Compounds **V** and **VI** are the oily substances stable on keeping isolated from air, the amidothionophosphate **V** is the most stable. Their structures were confirmed by ^{1}H and ^{31}P NMR spectroscopy. In ^{31}P NMR spectra we observed broadened singlet signals at δ_P 79.10 and 80.92 ppm, respectively. ^{1}H NMR spectra besides the signals of methylene protons of the backbone of the molecule (δ 3.25–4.31 ppm), broad singlet of methane protons in CHC_6H_5 group (δ 5.42 ppm) and signals of the protons of aromatic rings (δ 7.33–746 ppm) we observed resonance of methyl and methylene protons of the *N*-ethyl groups as typical triplet and quadruplet at δ 1.10 and 3.11 ppm, respectively.

For transfer to the models of lipids the phosphodiacetal **V** was treated with 75% acetic acid at 110°C to remove benzylidene prorecting groups. Yield of phosphotetraol **VII** was 75% [the conditions for removing acetal protecting groups were preliminary worked up on the example of transformation of diacetal **III** into parent dipentaerythritol **I** whose structure was confirmed by ^{1}H NMR spectrum, see (4)].

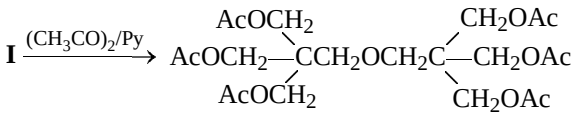
(4)



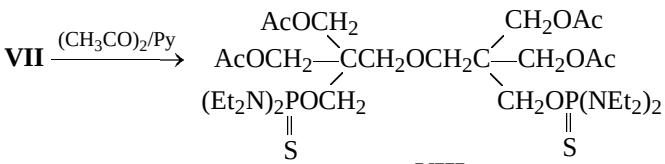
VII (5)

The ^{31}P NMR spectrum of compound **VII** contains a broad singlet at δ_P 80.10 ppm. Its ^{1}H NMR spectrum do not contain signals in the regions of δ 5.42 and 7.33–7.46 ppm of methine and aromatic protons in CHC_6H_5 group while at the δ 3.35 and 2.02 ppm appeared broad signals of methylene and hydroxyl protons in the hydroxymethyl groups.

In the final step of this work the phosphotetraol **VII** obtained was converted successfully to tetraacetate **IX** by the action of acetic anhydride in pyridine medium. The conditions for the total acylation of hydroxyl groups by acetic anhydride were preliminary worked up on the example of dipentaerythritol **I**, see (6).



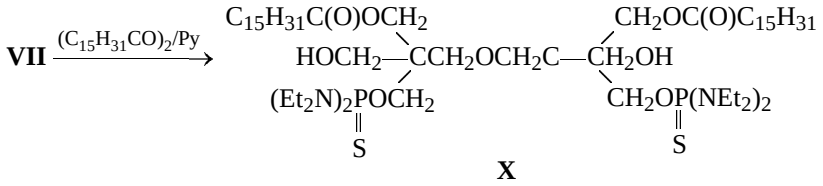
IX (6)



VIII (7)

Acetylation of phosphoerythritol **VII** proceeds at room temperature in 48 h, that of hexaol **I** in 12 h. Yield of terminal tetraacetyldiphospholipid **VIII** isolated by column chromatography was 78%. The ^{31}P NMR spectrum of diphospholipid **VIII** contains a broad peak at δ_P 79.84 ppm, in the same region as the parent tetraol **VII**. Structure of compounds **VIII** and **IX** is confirmed by ^1H NMR spectroscopy. Instead of the protons in hydroxyl groups, were registered singlets corresponding to methyl protons in acetyl groups, δ 1.78 and 1.67 ppm, respectively. Signals of methylene protons in $CH_3C(O)OCH_2$ groups are slightly shifted downfield as compared with the parent compounds **I** and **VII**. Other signals correspond to those of the oligools **I** and **VII**.

We attempted to perform complete acylation of phosphotetraol **VII** with a long-chain fatty acid anhydride, the palmic anhydride. The reaction was performed in pyridine at 25°C and at 80°C but regardless the conditions used, only two residues of the fatty acid was possible to introduce to the molecule of phosphotetraol **VII**.



(8)

X

Yield of this original lysophospholipid **X** prepared at 25°C and isolated by chromatography achieves 20% only. At 80°C the reaction proceeds for shorter period and yield rises to 30% but introducing of four acyl residues was not provided. Probably this is connected with the steric and other supramolecular requirements at the introduction of bulky residues of palmic acid.

The ^{31}P NMR spectrum of the phosphatid **X** contain a broad singlet at δ 79.82 ppm. Its ^1H NMR spectrum contains multiplets at δ 0.9–2.26 ppm related to methyl and methylene protons of residues of the fatty acid and at δ 1.78 ppm a triplet of hydroxyl groups is registered. Other signals in ^1H NMR spectrum correspond to the assigned structure of the compound (see Experimental).

Thus, on the basis of dipentaerythritol we prepared earlier unknown amidoditiophospate lipids containing two or four acyl residues of fatty acids. Such diphospholipid type compound can meet application in the study of structure and functions of model biomembranes. This mainly concerns the lisophospholipid **X** which by structure belongs to the group of lisophosphatides known as often responsible for the decay of cell membranes [18]. Also prospective is application of these products for creation of original supramolecular constructions interacting with other systems possessing specifically arranged long alkyl groups.

EXPERIMENTAL

The ^1H NMR spectra were registered on a Bruker WM-250 (250 MHz) instrument, chemical shifts are referred to HMDS (internal reference), the proton signal assignment was made on the basis of the data of double magnetic resonance. The ^{31}P–{^1H} spectra were obtained on a Bruker WP-80SY spectrometer with operating frequency 32.4 MHz relatively to external 85% phosphoric acid.

All the syntheses with trivalent phosphorus were performed under atmosphere of dry argon.

Adsorption chromatography was conducted on a column 15 mm diameter with silica gel L 100–250 μm, the R_f values were measured using TLC on Silufol UV-254 plates in the systems of benzene–dioxane 3:1 (A), hexane–dioxane 3:1 (B) and chloroform–methanol–water 65:25:4 (C). Melting points were determined in sealed capillary tubes with the heating rate 1 deg min^{-1}.

Phosphoric hexaethyltriamide was prepared by earlier described procedure [19]. The used compound coincided by constants with published one. Dipentaerythritol **I** from Acros Organics was prior to use recrystallized from water, mp 222–225°C.

2′,2″:6′,6″-Di-*O*-benzylidene-2′,2″,6′,6″-tetra-(hydroxymethyl)-4-oxa-1,7-heptanediol (III). *Method 1. Procedure for isolation a.* 1 g of dipentaerythritol **I** was mixed with 0.85 ml of freshly distilled benzaldeyde and 3 drops of concentrated hydrochloric acid was added. After homogenization the mixture was heated in vacuum 100 mm Hg at 90–95°C for 3 h, then cooled and dissolved in 20 ml of chloroform. Solution was filtered and filtrate was washed with 20 ml 1% K_2CO_3 to pH 7, the chloro-

form layer was separated and dried over anhydrous K_2CO_3 for 3 h. Then chloroform was removed in a vacuum and diacetal **III** was purified by chromatography on a column with silica gel (10 g) filled with benzene. Compound **III** was eluded with 30 ml of benzene–dioxane mixture 5 : 1. Solvents were removed in a vacuum and residue was kept for 2 h at 40°C (1 mm Hg). After chromatography yield of diacetal **III** 0.8 g (49%), mp 142–145°C, R_f 0.79 (A), 0.60 (B). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.36 br.s (2H, OH), 3.25 s, 3.36 s, 3.46 s (4H, CH_2OCH_2), 3.78 d (4H$_e$) and 4.10 d (4H$_a$) (C*H*$_2$OCH, ^2J(H$_a$H$_e$) 11.28 Hz), 3.84 d (4H, C*H*$_2$OH, $^3J_{HH}$ 6.41 Hz), 5.42 br.s (2H, C*H*C$_6$H$_5$), 7.35 br.s (6H, *-m*, *-p*) and 7.47 br.s (4H, *-o*) (C$_6$H$_5$). Found, %: C 67.14; H 7.03. $C_{24}H_{30}O_7$. Calculated, %: C 66.96; H 7.07. *M* 431.

Method 2. Procedure of isolation a. 0.5 g of dipentaerythritol **I** was suspended in 5 ml of DMF, 0.45 g of freshly distilled benzaldeyde and 3 drops of conc. HCl were added and the mixture was heated in vacuum 100 mm Hg at 90–95°C for 3 h. Diacetal **III** was isolated by column chromatography (see method *1*, procedure *a*). Yield 0.4 g (50%).

Procedure of isolation b. After cooling to room temperature, the reaction mixture was poured to 30 ml of 1% K_2CO_3. The suspension formed was kept for 3 h and precipitate was filtered off and dissolved in 30 ml of chloroform, the solution was dried over anhydrous K_2CO_3 for 3 h then solvent was removed in a vacuum and residue was kept for 3 h at 80°C (1 mm Hg). Yield of diacetal **III** 0.6 g (71%).

Method 3. Procedure of isolation b. 0.5 g of dipentaerythritol **I** was dissolved in 5 ml of DMSO, 0.45 g of freshly distilled benzaldeyde and 3 drops of conc. HCl were added and reaction mixture was heated in a vacuum (100 mm Hg) at 90–95°C 3 h and diacetal **III** was isolated in yield 0.5 g (61%) (see method *2*, procedure *b*).

Method 4. Procedure of isolation b. 0.5 g of dipentaerythritol **I** was dissolved in 5 ml of DMF–DMSO mixture 1 : 2 at 70–80°C in 0.5 h. Solution was cooled to 40–50°C and 0.45 g of freshly distilled benzaldeyde and 3 drops of conc. HCl were added. Then reaction mixture was heated in a vacuum (100 mm Hg) at 90–95°C for 3 h and diacetal **III** was isolated in yield 0.7 g (90%) (see method *2*, procedure *b*).

Method 5. Procedure of isolation b. By analogy with method *4*, from 0.5 g of dipentaerythritol **I** and 0.45 g of freshly distilled benzaldeyde in 5 ml of DMF–DMSO mixture 1 : 2 in the presence of 0.4 g of phosphotungstic acid ($H_3PO_4 \cdot 12WO_3 \cdot 24H_2O$) was obtained diacetal **III** in yield 0.6 g (75%) (see method *2*, procedure *b*).

Additional purification of 5,5'-[oxadi(methylene)-di-(5-hydroxymethyl-2-phenyl-1,3-dioxane)] (III) obtained in methods *1–5*.

(1) 0.3 g of diacetal **III** was dissolved in 3 ml of chloroform and precipitated by adding 5 ml of hexane. The precipitate was filtered off, washed with 2 ml of hexane and kept for 2 h at 40°C (1 mm Hg). Yield 0.27 g (90%), mp 142–145°C.

(2) 0.6 g of diacetal **III** was dissolved in 5 ml of benzene–dioxane mixture 3 : 1 and slowly cooled to room temperature (10 h). The precipitate formed was filtered off and kept for 2 h at 40°C (1 mm Hg). Yield 0.5 g (86%), mp 143–145°C.

(3) 0.7 g of diacetal **III** was dissolved in 8 ml of isopropyl alcohol and slowly cooled to room temperature (4 h). Precipitate was filtered off and kept for 2 h at 80°C (1 mm Hg). Yield 0.62 g (88.5%), mp 144–146°C.

1,7-Tetraethyldiamidothionophosphate-2',2'':6',6''-di-*O*-benzylidene-2',2'',6',6''-tetra(hydroxymethyl)-4-oxa-1,7-heptanediol (V). 0.3 g of acetal **III** and 0.3 g of phosphorous hexamethyltriamide (molar ratio 1 : 2) in 3 ml of anhydrous dioxane was stirred for 12 h at 25°C. Formation of amidophosphite **IV** was monitored by means of ^{31}P NMR spectroscopy. ^{31}P NMR spectrum (dioxane), δ_P, ppm: 134.74 br.s. To the reaction mixture was added 0.1 g of sulfur at room temperature and the mixture was kept for 3 h. The sulfur excess was filtered off, dioxane was removed in a vacuum. Diamidodithionodiphosphate **V** was purified on a column with silica gel (5 g) filled with hexane. Compound **V** was eluded with 30 ml of hexane–dioxane mixture 10 : 1. Solvents were removed in a vacuum and resudue was kept for 2 h at 40°C (1 mm Hg). Yield of compound **V** 0.42 g (72%), 1.5363, R_f 0.85 (A), 0.65 (B). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.10 t (24H, NCH_2CH_3, $^3J_{HH}$ 6.59 Hz), 3.11 q (16H, NCH_2CH_3, $^3J_{HP}$ 12.10 Hz), 3.25 s, 3.36 s, 3.50 s (4H, CH_2OCH_2), 3.83 m (4H*e*) and 4.31 m (4H$_a$) (C*H*$_2$OCH, ^2J(H$_a$H$_e$) 10.82 Hz), 4.15 m (4H, CH_2OP, $^3J_{HP}$ 10.96 Hz), 5.42 br.s (2H, C*H*C$_6$H$_5$), 7.35 br.s (6H, *-m*, *-p*) and 7.46 br.s (4H, *-o*) (C$_6$H$_5$). 31P NMR spectrum (dioxane), δ_P, ppm: 79.10 br.s. Found, %: C 56.83; H 8.09; P 7.41. $C_{40}H_{68}N_4O_7P_2S_2$. Calculated, %: C 56.98; H 8.13; P 7.35. *M* 843.

1,7-Tetraethyldiamidoselenonophosphate-2',2'':6',6''-di-*O*-benzylidene-2',2'',6',6''-tetra(hydroxymethyl)-4-oxa-1,7-heptanediol (VI) was prepared similarly to compound **V** from 0.3 g of diacetal **III**,

0.35 g of phosphorous hexaethyltriamide and 0.1 g of selenium. The selenium excess was filtered off and dioxane was removed in a vacuum. Diamidodiselenonediphosphate **VI** was purified by chromatography on a column with silica gel (5 g) filled with hexane. Compound **VI** was eluded with 25 ml of hexane–dioxane mixture 6 : 1, solvents were removed in a vacuum and residue was kept for 2 h at 40°C (1 mm Hg). Yield of compound **VI** 0.4 g (59%), 1.5429, R_f 0.90 (A), 0.47 (B). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.11 t (24H, NCH_2CH_3, $^3J_{HH}$ 6.10 Hz), 3.09 q (16H, NCH_2CH_3, $^3J_{HP}$ 12.29 Hz), 3.36 s, 3.46 s, 3.54 s (4H, CH_2OCH_2), 3.89 m ($4H_e$) and 4.27 m ($4H_a$) (CH_2OCH, $^2J(H_aH_e)$ 11.90 Hz), 4.14 m (4H, CH_2OP, $^3J_{HP}$ 11.95 Hz), 5.35 br.s (2H, CHC_6H_5), 7.36 br.s (6H, *-m*, *-p*) and 7.46 br.s (4H, *-o*) (C_6H_5). ^{31}P NMR spectrum (dioxane), δ_P, ppm: 80.92 br.s. and two broaden satellites, $^1J(^{31}P–^{77}Se)$ 837.06 Hz. Found, %: C 51.41; H 7.44; P 6.79. $C_{40}H_{68}N_4O_7P_2Se_2$. Calculated, %: C 51.28; H 7.32; P 6.61. *M* 937.

1,7-Tetraethyldiamidothionophosphate-2',2'',6',6''-tetra(hydroxymethyl)-4-oxa-1,7-heptanediol 2,2'-[Oxa(methylene)-di(2-methoxytetraethyldiamidothionophosphate-1,3-propandyl] (VII). Amidodithionodiphosphate **V**, 0.15 g, was placed to a round-bottom flask, 3 ml of 75% acetic acid was added and the mixture was heated with a reflux condenser at vigorous stirring for 13 h at 100–110°C to complete dissolving of compound **V**. Reaction mixture was then cooled to room temperature and diluted with equal amount of water (3 ml). The oil dropped was separated, washed with water (2 × 3 ml), dissolved in 5 ml of chloroform and dried over anhydrous K_2CO_3. After filtration, the solvent was removed in a vacuum and residue was kept for 3 h at 80–oC (1 mm Hg). Yield of compound **VII** 0.1 g (75%), 1.5490, R_f 0.10 (B), 0.75 (B). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.07 t (24H, NCH_2CH_3, $^3J_{HH}$ 7.02 Hz), 2.02 br.s (4H, OH), 3.05 q (16H, NCH_2CH_3, $^3J_{HP}$ 12.20 Hz), 3.35 br.s (8H, CH_2OH), 3.54 s (4H, CH_2OCH_2), 3.86 m (4H, CH_2OP, $^3J_{HP}$ 6.41 Hz). ^{31}P NMR spectrum (chloroform), δ_P, ppm: 80.10 br.s. Found, %: C 46.47; H 9.28; P 9.16. $C_{26}H_{60}N_4O_7P_2S_2$. Calculated, %: C 46.83; H 9.05; P 9.29. *M* 667. Phosphotetraol **VII** after drying of its solution in chloroform can be additionally purified on a column with silica gel (10 g) filled with hexane. Compound **VII** was eluded with 20 ml of hexane–dioxane mixture 3 : 1.

Preparation of 2',2'',6',6''-tetra(hydroxymethyl)-4-oxa-1,7-heptanediol (I) from dibenzylidenedipentaerythritol III. Diacetal **III**, 0.2 g, was suspended in 4 ml of 75% acetic acid and heated with reflux condenser at vigorous stirring for 1.5 h at 85–90°C to complete dissolution of compound **III**. Reaction mixture was then cooled to room temperature, diluted with equal volume of water (4 ml) and washed with hexane (2 × 10 ml) to transparency of aqueous layer. Water was removed in a vacuum and residue was kept for 3 h at 80°C (1 mm Hg). Yield of compound **I** 0.1 g (88%), mp 220–223°C (crude), 223–225°C (from H_2O), R_f 0.00 (B). ^{1}H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.28 br.s (4H, CH_2OCH_2), 4.19 d (12H, CH_2OH, $^3J_{HH}$ 5.50 Hz), 4.08 t (6H, CH_2OH, $^3J_{HH}$ 5.49 Hz). Found, %: C 47.41; H 8.95. $C_{10}H_{22}O_7$. Calculated, %: C 47.23; H 8.72. *M* 254.

2',2'',6',6''-Tetra-*O*-acetyl-1,7-tetraethyldiamidothionophosphate-2',2'',6',6''-tetra(hydroxymethyl)-4-oxa-1,7-heptanediol (VIII). Diphosphotetraol **VII**, 0.2 g, was dissolved at heating (50°C) in 5 ml of pyridine. To the solution cooled to room temperature was added 0.15 g of freshly distilled acetic anhydride and mixture was stirred for 48 h. Solution was then poured to cold water (0–1°C) the oil dropped was decanted, washed with cold water (2 × 10 ml), dissolved in chloroform and solution was dried over anhydrous K_2CO_3 for 3 h. Solvent was removed in a vacuum and compound **VIII** obtained was purified on a column with silica gel (5 g) filled with hexane. Compound **VIII** was eluded with 20 ml using hexane–dioxane 1 : 1 system. Solvents were removed in a vacuum and residue was kept for 2 h at 40°C (1 mm Hg). Yield of compound **VIII** 0.2 g (78%), 1.5513, R_f 0.78 (A), 0.49 (B). ^{1}H NMR spectrum (C_6D_6), δ, ppm: 1.02 t (24H, NCH_2CH_3, $^3J_{HH}$ 6.94 Hz), 1.78 s [12H, $CH_3(O)$], 3.03 q (16H, NCH_2CH_3 , $^3J_{HP}$ 12.19 Hz), 3.35 s, 3.42 s (4H, CH_2OCH_2), 4.28 d (4H, CH_2OP, $^3J_{HP}$ 12.06 Hz), 4.30 s [8H, $CCH_2OC(O)$]. ^{31}P NMR spectrum (chloroform), δ_P, ppm: 79.84 br.s. Found, %: C 48.78; H 8.01; P 7.38. $C_{34}H_{68}N_4O_{11}P_2S_2$. Calculated, %: C 48.90; H 8.21; P 7.42. *M* 835.

1,2',2'',6',6'',7-Hexa-O-acetyl -2',2'',6',6''-tetra(-hydroxymethyl)-4-oxa-1,7-heptanediol (IX) is prepared similarly to compound **VIII** from 0.15 g of pentaeritritol **I** and 0.25 g of acetic anhydride in the presence of 3 ml of pyridine in 12 h. The precipitate dropped at pouring to water was filtered off, washed with cold water (3 × 10 ml) and dried for 3 h at 80°C (1 mm Hg). Yield of compound **IX** 0.3 g (90%), mp 71–73°C, R_f 0.85 (A), 0.50 (B). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.05 s [18H, $CH_3(O)$], 3.18 s (4H, CH_2OCH_2), 4.14 s [12H, $CCH_2OC(O)$]. Found, %: C 52.23; H 6.84. $C_{22}H_{34}O_{13}$. Calculated, %: C 52.17; H 6.77. *M* 507.

2',6'-Dipalmoyl-1,7-tetraethyldiamidothionophosphate-2',6'-di(hydroxymethyl)-4-oxa-1,7-heptanediol (X) is prepared similarly to compound **VIII** from 0.1 g of diphosphotetraol **VII** and 0.2 g of

palmic anhydride in 2 ml of pyridine for 2 h at 50–70°C. Oily precipitate dropped in water was filtered off, washed with cold water (2 × 10 ml) and dissolved in 5 ml of chloroform. Insoluble admixture was filtered off, the filtrate wass dried over anhydrous K_2CO_3 for 3 h. Solvent was removed in a vacuum and residual compound **X** was purified on a column with silica gel (5 g) filled with hexane, eludedwith 10 ml of hexane–dioxane 5 : 1 system. Solvents were removed in a vacuum and residue was kept for 2 h at 40°C (1 mm Hg). Yield of compound **X** 0.05 g (30%), mp 14–15°C, R_f 0.53 (B). ^{1}H NMR spectrum (C_6D_6), δ, ppm: 0.92 t (6H, C*H*$_3$CH$_2$, $^3J_{HH}$ 6.7 Hz), 1.02 t (24H, NCH$_2$C*H*$_3$), 1.32 m [48H, CH$_3$(C*H*$_2$)$_{12}$], 1.65 m [4H, CH$_2$C*H*$_2$C(O)], 1.78 t (2H, CH$_2$OH, $^3J_{HH}$ 5.55 Hz), 2.26 m [4H, C*H*$_2$CH$_2$C(O)], 3.03 m (16H, NC*H*$_2$CH$_3$), 3.48 br.m (4H, CH$_2$OCH$_2$), 3.80 br.m (4H, CH$_2$OH), 4.17 br.m (4H, CH$_2$OP), 4.34 br.m [4H, CCH$_2$OC(O)]. ^{31}P NMR spectrum (benzene), δ_P, ppm: 79.82 br.s. Found, %: C 57.53; H 11.64; P 6.01. $C_{50}H_{120}N_4O_9P_2S_2$. Calculated, %: C 57.32; H 11.55; P 5.91. *M* 1048.

ACKNOWLEDGMENTS

This work was financially supported bythe President of Russian Federation (the Program of supporting advanced scientific schools of Russian Federation), grant NSh-5515.2006.3.

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