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Tris-Phosphorylated Esters of Symmetrical and Unsymmetrical Triols

N. M. Pugashova[a], A. M. Koroteev[a], I. S. Bushmarinov[b], K. A. Lysenko[b], E. N. Andriutse[a], M. P. Koroteev[a], and E. E. Nifant'ev[a]

[a] *Moscow Pedagogical State University*
Nesvizhskii per., 3, Moscow119021, Russia
e-mail: mpkoroteev@mail.ru

[b] *Institute of Organoelemental Compounds, Russian Academy of Sciences, Moscow, Russia*

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Abstract—By reaction of a series of triols and monosaccharides with 5,5-dimethyl-2-chloro-1,3,2-dioxaphosphorinane their tris-phosphorylated derivatives were synthesized, and the simplest chemical transformations of the latter were studied. Structures of the obtained P(V) derivatives were confirmed by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy and by the MALDI TOF mass spectrometry and X-ray structural analysis.

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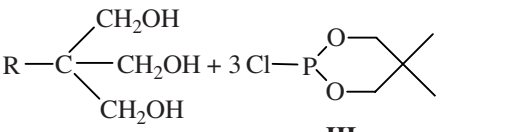
Up till now bis-phosphorylated polyol systems including two phosphorus atoms are well studied [1–3] while the systems with three and more phosphoric nodes are poorly documented. Investigation of trends in the synthesis and reactivity features of such compounds may provide promising ligands for designing new types of catalysts, extraction agents and other practically important products. This communication describes the results of studying exhaustive phosphorylation of a series of triols.

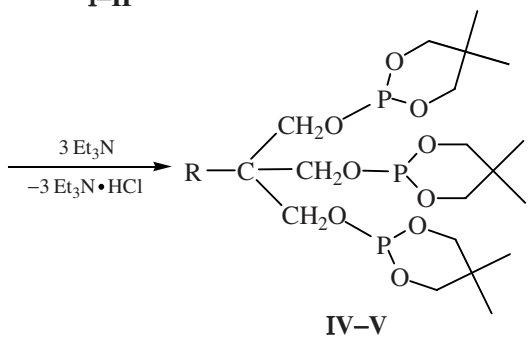
In the first step of this investigation simplest 1,1,1-trimethylolalkanes, metriol (**I**) and etriol (**II**), were chosen as a matrix for the polyphosphorylation. Due to the presence of symmetrically located primary hydroxy groups these triols are promising substrates for obtaining sterically loaded systems. There are no steric hindrances to their phosphorylation, therefore these syntheses should proceed effectively under mild conditions and with a high yield.

We prepared tris-phosphorylated 1,1,1-trimethylolalkane esters **I, II** by reaction of the corresponding triol with three-fold equivalent amount of 5,5-dimethyl-2-chloro-1,3,2-dioxaphosphorinane ("neopentylchlorophosphite") in the presence of triethylamine at room temperature. As a solvent for the synthesis of tris-phosphites **IV** and **V** carbon tetrachloride or dioxane was used. Choice of these solvents was governed by the difference in solubility of the parent triols. Reaction progress was monitored by TLC and ^{31}P NMR spectroscopy. We found that the completion of triols phosphorylation occurred in 1.5 h after mixing the initial reagents. In the ^{31}P NMR spectra of the reaction mixtures after reaction completion were registered singlet signals in the regions of 122 or 121 ppm for the compounds **IV** or **V**,

Scheme 1.



I–II **III**



IV–V

R = CH_3 (**I, IV**); C_2H_5 (**II, V**).

respectively, that corresponded to the phosphates based on neopentylene glycol [4]. Existence of a single signal in each case reveals the high symmetry of the system that leads to magnetic equivalence of all phosphorus nuclei.

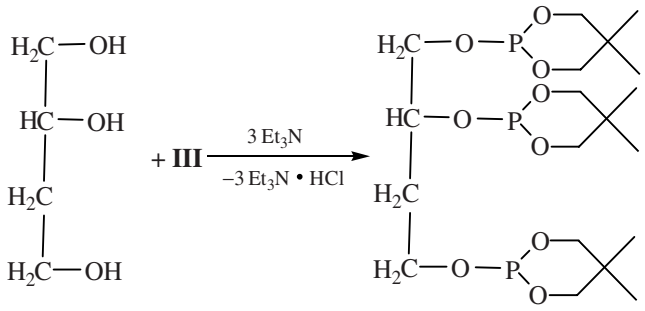
Yield of tris-phosphite from metriol **IV** was 92%, from etriol derivative **V**, 93%, judging from the integral intensities in the ^{31}P NMR spectra. Phosphites **IV** and **V** after removing from the reaction mixture triethylamine hydrochloride and solvent were characterized by ^{13}C NMR spectroscopy (see Experimental).

Besides, we carried out complete phosphorylation of unsymmetrical 1,2,4-butanetriol. Reaction conditions and the monitoring of the reaction process are analogous to those in preceding experiments. In the ^{31}P NMR spectrum of the reaction mixture were registered three singlet signals of equal intensities with chemical shifts 123.4, 124.0 and 124.3 ppm that confirmed indirectly nonequivalence of hydroxy groups in the parent triol.

Yield of tris-phosphite **VII** by the data of ^{31}P NMR spectroscopy was only 58%, probably die to steric hindrances for the phosphorylation at the secondary hydroxy group of trihydroxybutane.

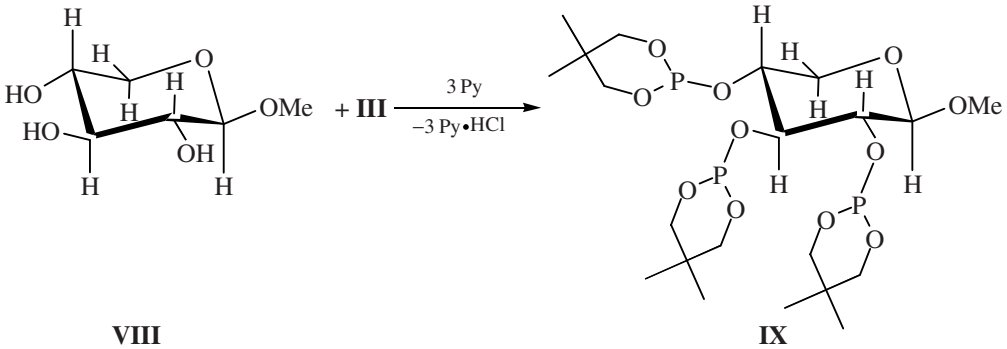
In the second step of this investigation we studied synthesis of tris-phosphites based on heavier triols, partially protected monosaccharides, 1,2-*O*-alkylidene-glucofuranose and methyl β-*D*-xylopyranoside. We found that tris-phosphites from these compounds were formed in the reaction of the parent triol with 5,5-dimethyl-2-chloro-1,3,2-dioxaphosphorinane in the 1 : 3 ratio. The syntheses were carried out at stirring and cooling to 5°C of the reaction mixtures with dioxane as solvent. As an acceptor of hydrogen chloride were used either pyridine or triethylamine. After charging neopentylenechlorophosphite the mixture was additionally stirred for 1 h at room temperature, because in these cases reaction proceeded slower than in the syntheses of tris-phosphites **IV**, **V,** and **VII**.

Scheme 2.

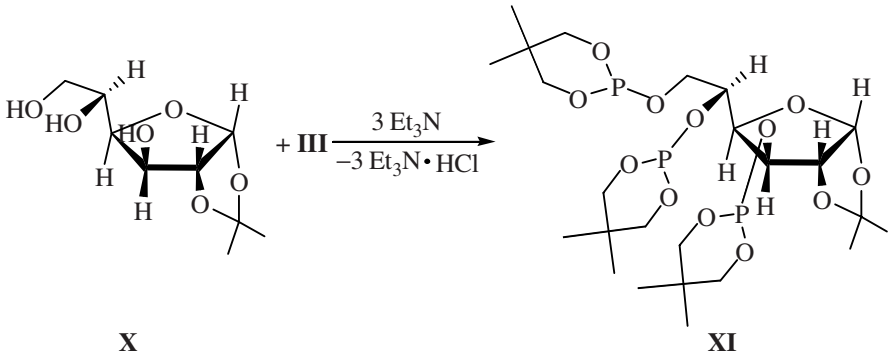


VI **VII**

Scheme 3.



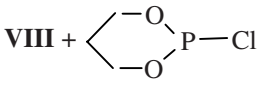
VIII **IX**



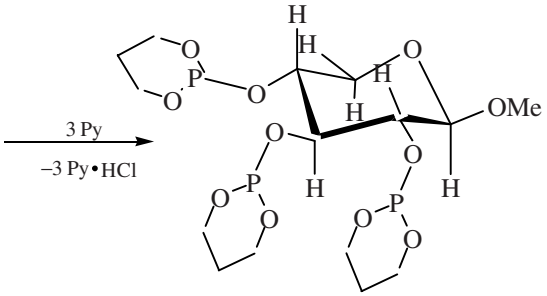
X **XI**

The reaction progress was monitored by TLC and ^{31}P NMR spectroscopy. In the ^{31}P NMR spectra of reaction mixtures after reaction completion, in both cases were registered three singlet signals in the region of 121–123 ppm. Yields of compounds **IX** and **XI** were 72 and 76%, respectively. Similarly, at the treatment of the methyl-β-*D*-xylopyranoside with 2-chloro-1,3,2-dioxaphosphorinane ("propylenechlorophosphite") we obtained tris-phosphite (**XIII**). The phosphorus nuclei in the latter resonated at δ_P 127.7, 128.1, and 129.5 ppm.

Scheme 4.



XII



XIII

Yield of the phosphite by the data of ^{31}P NMR spectroscopy was 69%. Thus, we can conclude that the selected triols based on the partially protected carbohydrates **VIII** and **X** afford the corresponding tris-phosphites **IX**, **XI** and **XIII** fairly readily. Despite the steric hindrances, this reaction proceeds under mild conditions. However, we have to note that the synthesized phosphites are not stable enough under the conditions of their isolation (chromatography, crystallization). Therefore they were transformed into compounds with pentavalent phosphorus atom.

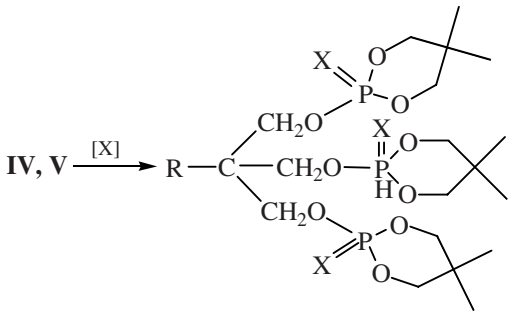
For instance, phosphorylated esters **IV** and **V** were isolated and characterized as the corresponding phosphates, thionophosphates, and selenophosphates. These compounds are stable crystalline substances.

Oxidation of tris-phosphorylated esters **IV** and **V** with urea-hydrogen peroxide adduct was carried out at room temperature in methylene chloride with two-fold excess of the oxidizer. Reaction process was monitored by ^{31}P NMR spectroscopy.

To the reaction completion in the ^{31}P NMR spectra of reaction mixture the signals of parent phosphites were absent but singlet signals were registered in the region of –8 ppm characteristic of this kind phosphates [4].

Sulfuration and selenation of compounds **IV** and **V** was achieved by keeping the mixture of reacting substances for 1.5–2 h at room temperature. As a solvent for sulfuration was used benzene, for selenation, dioxane. After completing the process, in the ^{31}P NMR spectra of reaction mixtures singlet signals in the region 60–61 ppm were observed characteristic of thiophosphates and, respectively, in the region 64–65 ppm characteristic of selenophosphates [4].

Scheme 5.



XIV–XIX

R = CH_3, X = O (**XIV**); S (**XV**); Se (**XVI**); R = C_2H_5, X = O (**XVII**); S (**XVIII**); Se (**XIX**).

Under the reaction conditions the target derivatives with pentavalent phosphorus precipitated from the reaction mixtures, and their isolation was thus simplified. Tris-phosphates **XIV** and **XVII**, tris-thionophosphates **XV** and **XVIII,** and tris-selenophosphates **XVI** and **XIX** were isolated in high yields and were characterized. They are white powders with high melting points (see Table 1 and Experimental)

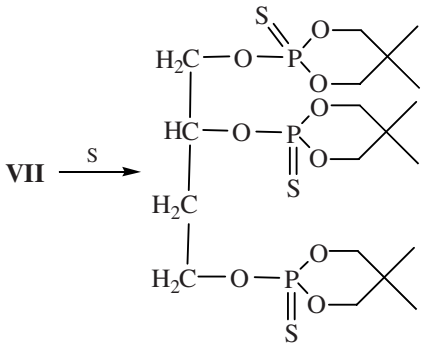
To obtain stable derivative of tris-phosphorylated polyol **VII** excess sulfur was added to this compound, and the mixture was left overnight. After completion of the process in the ^{31}P NMR spectrum a signal characteristic of neopentylene glycol thionophosphate was observed in the region of δ_P 61 ppm.

Obtained compound **XX** was isolated by column chromatography on silica gel in 36% yield. Structures of the synthesized compounds **XIV**–**XX** were also confirmed by elemental analysis and ^{1}H and ^{13}C NMR spectra. The spectra contained signals of all proton groups with appropriate intensity and the expected sets

Table 1. Characteristic parameters of compounds **XIV**–**XXIII**

Compound	X	Yield, %	mp, °C	δ_P, ppm
XIV	O	81	202–204	–7.4
XV	S	71	202–203	60.8
XVI	Se	65	166–168	65.1 (J_{PSe} 987 Hz)
XVII	O	75	208–210	–8.5
XVIII	S	94	202–204	61.1
XIX	Se	65	168–170	64.4 (J_{PSe} 987 Hz)
XX	S	36	125–126	60.7, 61.1, 61.4
XXI	S	31	158–160	61.5, 62.8, 63.1
XXII	S	27	152–153	63.2, 64.5, 65.1
XXIII	S	32	139–140	59.7, 60.1, 60.4

Scheme 6.

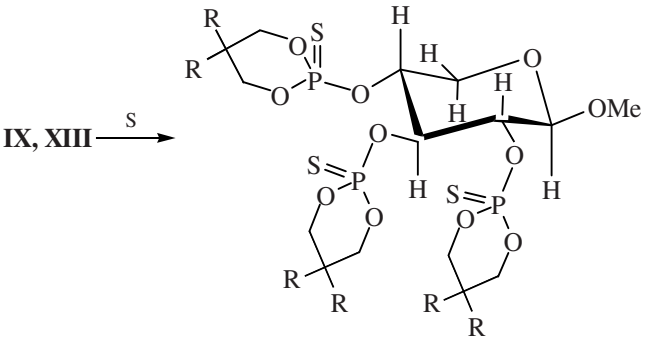


XX

of the signals of carbon nuclei. Composition of tris-phosphorylated butanetriol derivative **XX** was also proved by the MALDI TOF method. In the mass spectrum thus obtained a well expressed peak is observed with mass number 621 corresponding to molecular ion [M + Na^+] (see Experimental), and fragmentation peaks of this compound.

We found that the tris-phosphites derived from carbohydrates (**IX**, **XI** and **XIII**) add sulfur under more rigid conditions, therefore to these tris-phosphites was added crystalline sulfur in excess at short heating and then reaction mixtures were left overnight. After completion of the process, in the ^{31}P NMR spectra signals characteristic of thionophosphates were registered: from thionophosphate **XXI** appeared a group of signals in the region of 63–65 ppm, and from phosphate **XXII** were observed three signals with chemical shifts 61.5, 62.8 and 63.0 ppm.

Scheme 7.

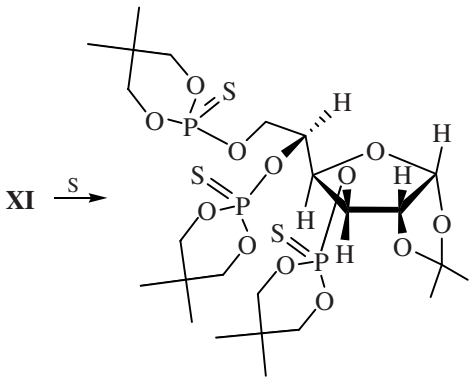


XXI, XXII

R = H (**XXI**); R = Me (**XXII**).

In the spectrum of tris-thionophosphate from glucose **XXIII** were observed three signals in the region of 60–61 ppm of equal intensity, evidencing formation of this product.

Scheme 8.



XXIII

Thiophosphates **XXI**–**XXIII** were isolated in individual state by column chromatography on silica gel. The obtained compounds are white solid substances with high melting points. Their structures were confirmed by ^1H and ^{13}C NMR spectroscopy and elemental analysis. By the MALDI TOF method was measured the molecular mass of compound **XXII**. The mass of molecular ion was m/z = 678 $[M^+ + Na^+]^+$.

Unambiguous evidence of the structure of tris-thiophosphate **XXI** was obtained by X-ray diffraction analysis. The general view of molecule **XXI** is shown in the figure, the principal bond lengths and bond angles are listed in Table 2. In crystal of compound **XXI** methyl-β-*D*-xylopyranoside fragment of the molecule is in the *chair* $^4C_1$ conformation with devia-

tion of O^5 and C^3 atoms 0.702(3) and –0.606(4) Å, respectively, from the plane formed by the atoms $C^1C^2C^4C^5$ (average deviation 0.01 Å).

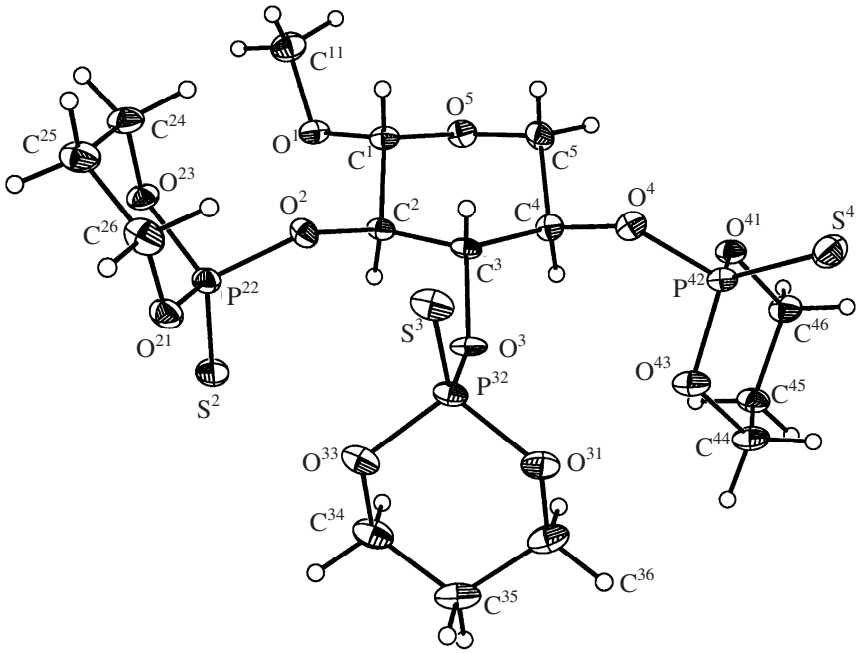
All three dioxathionophosphate fragments of the molecule are characterized by the same conformation of screwed chair with deviation of phosphorus and C^{n5} atoms (C^{25}, C^{35} and C^{45}, see the figure) from the planes of remaining atoms of the ring (average deviation varies in the range 0.005–0.02 Å) by 0.60–0.72 Å.

Phosphorus atoms in the structure are characterized by slightly distorted tetrahedral configuration with bond angles in the range 101.1(1)°–117.1(1)° with systematic decrease in endocyclic OPO angles and increase in exocyclic OPS angles. The bond lengths and bond angles in dioxathionophosphate rings are close by value and correspond to published data for such systems [5]. Noteworthy that the mutual positions of dioxathionophosphate rings and central pyranose ring for three independent fragments are different. Actually, the values of torsion angles $S^2P^{22}O^2C^2$, $S^3P^{32}O^3C^3$, and $S^4P^{42}O^4C^4$ are 26.6(2), –5.4(2) and 172.91(18)°, respectively. Therewith, the difference in torsion angles leads to change in character of possible stereoelectronic interactions of oxygen atoms O^2, O^3 and O^4. Thus, in the case of dioxathionophosphate fragment in the 4th position of pyranose ring the lone electron pairs (*lp*) of the atom O^4 and endocyclic P–O bonds are in antiperiplanar position that promotes charge transfer $lp_{O^4}\rightarrow\sigma^*(P^{42}–O^{41})$, $lp_{O^4}\rightarrow\sigma^*(P^{42}–O^{43})$ (pseudo-torsion angles $lpO^4P^{42}O^{41}$ and $lpO^4P^{42}O^{43}$ are 170.2 and 176.1°, respectively), while for two other dioxathionophosphate substituents such interaction is either impossible, or is much weaker because the respective pseudotorsion angles *lp*OPO are 140° only or less. Existence of these stereoelectronic interactions involving lone electron pairs of oxygen atom O^4 follows from contraction of $P^{42}–O^4$ bond length [1.573(2) Å] by 0.026 Å as compared to the bonds $P^{32}–O^3$ [1.599(2) Å] and $P^{22}–O^2$ [1.599(2) Å], and some elongation of bonds P^{42}–O in the rings (see Table 2.). Difference in the orientation of dioxathionophosphate fragments probably is defined by the scope of weak van der Waals interactions in the crystal.

Thus, we first synthesized a series of earlier unknown esters containing three phosphorus atoms, investigated their structure and showed that cyclic phosphites of triols and monosaccharides show high reactivity in oxidation and sulfuration.

EXPERIMENTAL

All experiments with trivalent phosphorus compounds were carried out under nitrogen atmosphere using carefully dried solvents. The ^{31}P NMR spectra



General view of 2,3,4-Tris-(2'-thio-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)methyl-β-*D*-xylopyranoside (**XXII**) .

Table 2. Selected values of bond length (*d*, Å) and bond angles (ω, deg) of compound **XXI**

Bond	*d*	Bond	*d*
S^2–P^{22}	1.9061(11)	P^{42}–O^{41}	1.584(2)
S^3–P^{32}	1.9125(10)	P^{42}–O^{43}	1.589(2)
S^4–P^{42}	1.9127(11)	O^1–C^1	1.376(3)
P^{22}–O^{21}	1.573(2)	O^1–C^{11}	1.427(4)
P^{22}–O^{23}	1.579(2)	O^2–C^2	1.435(3)
P^{22}–O^2	1.599(2)	O^3–C^3	1.446(3)
P^{32}–O^{31}	1.573(2)	O^4–C^4	1.448(3)
P^{32}–O^{33}	1.577(2)	O^5–C^5	1.427(3)
P^{32}–O^3	1.594(2)	O^5–C^1	1.432(3)
P^{42}–O^4	1.573(2)		
Angle	ω	Angle	ω
$O^{21}P^{22}O^{23}$	105.30(12)	$O^{41}P^{42}S^4$	116.57(9)
$O^{21}P^{22}O^2$	101.12(11)	$O^{43}P^{42}S^4$	116.21(9)
$O^{23}P^{22}O^2$	104.20(11)	$C^1O^1C^{11}$	113.4(2)
$O^{21}P^{22}S^2$	114.57(9)	$C^2O^2P^{22}$	125.63(17)
$O^{23}P^{22}S^2$	113.47(9)	$C^3O^3P^{32}$	125.59(17)
$O^2P^{22}S^2$	116.68(8)	$C^4O^4P^{42}$	122.98(17)
$O^{31}P^{32}O^{33}$	105.08(12)	$C^5O^5C^1$	110.6(2)
$O^{31}P^{32}O^3$	102.51(11)	$C^{26}O^{21}P^{22}$	118.56(18)
$O^{33}P^{32}O^3$	103.41(12)	$C^{24}O^{23}P^{22}$	116.83(18)
$O^{31}P^{32}S^3$	114.05(9)	$C^{36}O^{31}P^{32}$	117.79(19)
$O^{33}P^{32}S^3$	113.27(9)	$C^{34}O^{33}P^{32}$	118.16(18)
$O^3P^{32}S^3$	117.08(8)	$C^{46}O^{41}P^{42}C$	115.79(18)
$O^4P^{42}O^{41}$	102.74(11)	$C^{44}O^{43}P^{42}$	114.87(19)
$O^4P^{42}O^{43}$	104.01(12)	$O^1C^1O^5$	109.1(2)
$O^{41}P^{42}O^{43}$	103.45(11)	$O^1C^1C^2$	108.2(2)
$O^4P^{42}S^4$	112.21(9)	$O^5C^1C^2$	108.9(2)

were registered on a Bruker WP-80 SY instrument with operating frequency 32.4 MHz, relatively to 85% orthophosphoric acid. The ^{13}C and ^1H NMR spectra were registered on a Bruker AC-200 instrument with operating frequencies 50.32 and 200 MHz. respectively, relatively to tetramethylsilane. The ^1H, ^{13}C and ^{31}P NMR spectra of compounds **V** and **XV** and **XIX** were additionally registered on a Bruker AVANCE-400 instrument with operating frequencies 161.98 (^{31}P), 100.61 (^{13}C) and 400.13 MHz (^1H). For elemental analysis was used automatic analyzer Perkin-Elmer-2400. Measuring of monoisotopic (^{12}C) molecular masses was realized on a Bruker UltraFlex (Bruker Daltomics, Germany) instrument.

Colorless crystals of compound **XXI** have been grown from benzene. At100 K the crystals of **XXI** are rhombic, space group $P2_12_12_1$, *a* 8.1904(7), *b* 12.827(1), *c* 22.951(2) Å, *V* 2411.4(4) Å^3, *Z* 4 (*Z*' 1), $d_{calc.}$ 1.577 g cm^{-3}, μ(MoK_α) 0.559 cm^{-1}, *F*(000) 1192. Intensities of 16 999 reflexes were measured at the tem-perature 100 K on a Bruker SMART APEX II CCD diffractometer [λ(MoK_α) 0.71073 Å, ω-scan, 2θ < 60°], 6836 independent reflexes (R_{int} 0.0527) were used for further refinement. Structure was solved by the direct method and consecutive syntheses of electron density. Positions of hydrogen atoms were determined from difference Fourier syntheses. Refinement was carried out on F^2_{hkl} in anisotropic approximation for nonhydrogen atoms and isotropically for hydrogen atoms. Positions of hydrogen atoms were refined using *rider* model.

Absolute configuration of crystal **XXI** is confirmed on the basis of the Flack parameter that had value of 0.03(7). Final values of reliability factors for **XXI** are: *R*1 0.0458 [calculated from F_{hkl} for 5590 reflexes with $I > 2\sigma(I)$], *wR*2 0.0906 (calculated from F^2_{hkl} for all 6836 reflexes), the number of refined parameters 290, GOF 1.011. Calculations were carried out using program package SHELXTL 5.10. [6].

For thin layer chromatography were used plates Silufol UV-254. Eluents benzene–dioxane, 3 : 1 (A) and benzene–dioxane, 5 : 1 (B).

5,5-Dimethyl-2-chloro-1,3,2-dioxaphosphorinane, 2-chloro-1,3,2-dioxaphosphorinane [7] and 1,2-*O*-alkylideneglucofuranose [8] were synthesized along the known procedures. Methyl-β-*D*-xylopyranoside from Sigma and 2,2-dimethyl-1,3-propanediol from Fluka Chemie were used without additional purification.

General procedure for the synthesis of tris-phosphorylated esters of 1,1,1-trimethylolalkanes (IV, V). To a mixture of an appropriate triol with triethylamine in equimolar amounts dissolved in 5–10-fold excess of a solvent and cooled to 5–10°C was slowly added dropwise at stirring 10–15% solution of

three-fold molar excess of 5,5-dimethyl-2-chloro-1,3,2-dioxaphosphorinane. As a solvent was taken carbon tetrachloride or 1,4-dioxane. The reaction progress was monitored by ^{31}P NMR spectroscopy and TLC. The mixture was stirred at room temperature for 1.5 h. The triethylamine hydrochloride precipitate was filtered off, the filtrate was concentrated in a vacuum (20 mm Hg.). The product was extracted with benzene, the solvent was removed, and residue was dried in a vacuum (1 mm Hg) at 50°C to a constant weght.

1,1,1-Tris-hydroxymetylene-(5',5'-dimethyl-1',3',2'-dioxaphosphorinane)ethane (IV). From 0.31 g of 1,1,1-trimethylolethane (**I**), 0.79 g of triethylamine and 1.32 g of 5,5-dimethyl-2-chloro-1,3,2-dioxaphosphorinane was obtained ester **IV**. Yield 1.23 g, syruplike liquid, R_f 0.81 (A). ^{13}C NMR spectrum (CD_3CN), δ, ppm (*J*, Hz): 7.9 (CH_3), 19.5 (CH_3^e), 20.5 (CH_3^a), 31.8 [$C(CH_3)_2$, $^3J_{CP}$ 6.7], 45.7 (CH_3C, $^3J_{CP}$ 8.9), 68.5 (CH_2OP, $^2J_{CP}$ 5.1), 77.6 [$CH_2C(CH_3)_2$, $^2J_{CP}$ 6.7].

1,1,1-Tris-hydroxymetylene-(5',5'-dimethyl-1',3',2'-dioxaphosphorinane)propane (V). From 0.27 g of 1,1,1-trimethylolpropane (**II**), 0.61 g of triethylamine and 1.01 g of 5,5-dimethyl-2-chloro-1,3,2-dioxaphosphorinane was obtained ester **V**. Yield 0.98 g, syruplike liquid, R_f 0.9 (A). ^{13}C NMR spectrum [$(CD_3)_2SO$], δ, ppm (*J*, Hz): 7.9 (CH_3CH_2), 20.3 (CH_3^e), 20.7 (CH_3CH_2), 20.9 (CH_3^a), 32.0 [$C(CH_3)_2$, $^3J_{CP}$ 6.7], 45.8 (CH_3C, $^3J_{CP}$ 9.1), 71.3 (CH_2OP, $^2J_{CP}$ 5.4), 76.3 [$CH_2C(CH_3)_2$, $^2J_{CP}$ 8.3].

General procedure for the synthesis of 1,1,1-tris-hydroxymethylene-(5',5'-dimethyl-1',3',2'-dioxaphosphorinane)alkanes (XIV, XVII). To a solution of an appropriate tris-phosphorylated ester in 5-fold excess of carbon tetrachloride was added two-fold excess of hydrogen peroxide adduct with urea, and the mixture was stirred for 4 h at 20°C. The precipitate formed was filtered off, washed with the same solvent, then the solvent was removed in a vacuum, the residue was extracted with hot benzene (2 × 15 ml). Benzene was removed in a vacuum (20 mm Hg) to the beginning of product crystallization, crystals formed were filtered off and tris-phosphates obtained were dried in a vacuum (1 mm Hg) at 90°C to a constant weight.

1,1,1-Tris-hydroxymetylene-(2'-oxo-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)ethane (XIV). From 1.29 g of ester **IV** and 1.41 g of hydrogen peroxide adduct with urea was obtained phosphate **XIV**. Yield 1.14 g, white crystalline substance. ^{13}C NMR spectrum (CD_3CN), δ, ppm (*J*, Hz): 7.8 (CH_3), 19.4 (CH_3^e), 20.5 (CH_3^a), 31.4 [$C(CH_3)_2$, $^3J_{CP}$ 6.3], 45.5 (CH_3C, $^3J_{CP}$ 8.5), 68.3 (CH_2OP, $^2J_{CP}$ 4.9), 77.7 [$CH_2C(CH_3)_2$, $^2J_{CP}$ 6.6]. ^{1}H NMR spectrum (CD_3CN), δ, ppm: 0.82 s (9H, CH_3^e), 1.05 s (9H, CH_3^a), 1.23 s (3H, CH_3), 3.72 m (6H, OCH_2^e), 3.96 m (6H, CH_2OP), 4.16 m (6H, OCH_2^a). Found, %: C 42.51; H 6.85; P 16.42; $C_{20}H_{39}O_{12}P_3$. Calculated, %: C 42.55; H 6.91; P 16.49.

1,1,1-Tris-hydroxymetylene-(2'-oxo-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)propane (XVII). From 1.26 g of ester **V** and 1.34 g of hydrogen peroxide adduct with urea was obtained phosphate **XVII**. Yield 1.03 g, white crystalline substance. ^{13}C NMR spectrum [$(CD_3)_2CO$], δ, ppm (*J*, Hz): 7.6 (CH_3CH_2), 20.7 (CH_3^e), 21.5 (CH_3CH_2), 21.8 (CH_3 *a*), 32.2 [$C(CH_3)_2$, $^3J_{CP}$ 6,3], 43.2 (C_2H_5C, $^3J_{CP}$ 8,9), 65.5 (CH_2OP, $^2J_{CP}$ 4.5), 78.4 [$CH_2C(CH_3)_2$, $^2J_{CP}$ 5.33]. ^{1}H NMR spectrum [$(CD_3)_2CO$], δ, ppm: 0.83 s (9H, CH_3^e), 0.85 t (3H, CH_3), 0.89 s (9H, CH_3^a), 1.38 q (2H, CH_2), 3.54 m (6H, OCH_2^e), 4.57 m (6H, CH_2OP), 4.61 m (6H, OCH_2^a). Found, %: C 43.55; H 7.05; P 16.03; $C_{21}H_{41}O_{12}P_3$. Calculated, %: C 43.60; H 7.09; P 16.09.

General procedure for the synthesis of 1,1,1-tris-hydroxymethylene-(2'-thio-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)alkanes (XV, XVIII) and 1,1,1-tris-hydroxymethylene-(2'-seleno-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)alkanes (XVI, XIX). To a solution of the respective tris-phosphorylated ester in 10-fold excess of benzene was added sulfur or selenium in equivalent amount, and the mixture was stirred at 20°C. Reactions duration: of sulfuration, 1 h, of selenation, 5 h. The precipitate formed was filtered off and washed with the same solvent (2 × 15 ml). Thionophosphates were precipitated from the reaction mixture by adding methyl-*tert*-butyl ether, selenonophosphates, by hexane. The products were recrystallized from hot toluene and dried in a vacuum (1 mm Hg) at 70°C to a constant weight.

1,1,1-Tris-hydroxymetylene-(2'-thio-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)ethane (XV). From 0.51 g of ester **IV** and 0.09 g of sulfur was obtained thionophosphate **XV**. Yield 0.42 g, white crystalline substance. ^{13}C NMR spectrum (CD_3CN), δ, ppm (*J*, Hz): 7.9 (CH_3), 19.5 (CH_3^e), 20.6 (CH_3^a), 31.9 [$C(CH_3)_2$, $^3J_{CP}$ 6.3], 45.7 (CH_3C, $^3J_{CP}$ 8.9), 68.5 (CH_2OP, $^2J_{CP}$ 4.9), 77.9 [$CH_2C(CH_3)_2$, $^2J_{CP}$ 6.6]. ^{1}H NMR spectrum (CD_3CN), δ, ppm: 0.94 s (9H, CH_3^e), 1.12 s (9H, CH_3^a), 1.25 s (3H, CH_3), 3.97 m (6H, OCH_2^e), 4.08 m (6H, CH_2OP), 4.21 m (6H, OCH_2^a). Found, %: C 39.17; H 6.31; P 15.16; $C_{20}H_{39}O_9P_3S_3$. Calculated, %: C 39.22; H 6.37; P 15.20.

1,1,1-Tris-hydroxymetylene-(2'-thio-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)propane (XVIII). From 1.05 g of ester **V** and 0.18 g of sulfur was obtained thionophosphate **XVIII**. Yield 1.1 g, white crystalline substance. ^{13}C NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.2 (CH_3CH_2), 20.8 (CH_3^e), 21.5 (CH_3CH_2), 21.8 (CH_3^a), 32.4 [$C(CH_3)_2$, $^3J_{CP}$ 6,3], 43.3 (C_2H_5C, $^3J_{CP}$ 8.9), 65.6 (CH_2OP, $^2J_{CP}$ 4.5), 77.7 [$CH_2C\cdot(CH_3)_2$, $^2J_{CP}$ 7.4]. ^{1}H NMR spectrum (CD_3CN), δ, ppm: 0.94 s (9H, CH_3^e), 0.98 s (9H, CH_3^a), 1.10 t (3H, CH_3), 1.51 q (2H, CH_2), 3.87 m (6H, CH_2OP), 3.98 m (6H, OCH_2^e), 4.06 m (6H, OCH_2^a). Found, %: C 40.21; H 6.48; P 14.84; $C_{21}H_{41}O_9P_3S_3$. Calculated, %: C 40.26; H 6.55; P 14.86.

1,1,1-Tris-hydroxymetylene-(2'-seleno-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)ethane (XVI). From 0.52 g of ester **IV** and 0.27 g of selenium was obtained selenonophosphate **XVI**. Yield 0.48 g, white crystalline substance. ^{13}C NMR spectrum (CD_3CN), δ, ppm (*J*, Hz): 7.9 (CH_3), 19.6 (CH_3^e), 20.6 (CH_3^a), 31.9 [$C(CH_3)_2$, $^3J_{CP}$ 6.4], 45.7 (CH_3C, $^3J_{CP}$ 8.9), 68.6 (CH_2OP, $^2J_{CP}$ 4.9), 77.9 [$CH_2C(CH_3)_2$, $^2J_{CP}$ 6.7]. ^{1}H NMR spectrum (CD_3CN), δ, ppm: 0.95 s (9H, CH_3^e), 1.12 s (9H, CH_3^a), 1.29 s (3H, CH_3), 3.99 m (6H, OCH_2^e), 4.11 m (6H, CH_2OP), 4.25 m (6H, OCH_2^a). Found, %: C 31.81; H 5.14; P 12.33; $C_{20}H_{39}O_9P_3Se_3$. Calculated, %: C 31.87; H 5.18; P 12.35.

1,1,1-Tris-hydroxymetylene-(2'-seleno-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)propane (XIX). From 1.26 g of ester **V** and 0.56 g of selenium was obtained selenonophosphate **XIX**. Yield 1.17 g, white crystalline substance. ^{13}C NMR spectrum [$(CD_3)_2SO$], δ, ppm (*J*, Hz): 8.7 (CH_3CH_2), 20.3 (CH_3^e), 20.8 (CH_3CH_2), 20.9 (CH_3^a), 32.0 [$C(CH_3)_2$, $^3J_{CP}$ 6.3], 45.7 (C_2H_5C, $^3J_{CP}$ 8.9), 71.7 (CH_2OP, $^2J_{CP}$ 5.6), 76.7 [$CH_2C\cdot(CH_3)_2$, $^2J_{CP}$ 8.7]. ^{1}H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 0.88 t (3H, CH_3), 0.99 s (9H, CH_3^e), 1.13 s (9H, CH_3^a), 1.41 q (2H, CH_2), 3.56 m (6H, CH_2OP), 3.85 m (6H, OCH_2^e), 4.19 m (6H, OCH_2^a). Found, %: C 32.81; H 5.31; P 11.95; $C_{21}H_{41}O_9P_3Se_3$. Calculated, %: C 32.86; H 5.35; P 12.10.

General procedure for the synthesis of trisphosphorylated derivatives of carbohydrates and 1,2,4-butanetriol (XX–XXIII). To the cooled to 0–5°C mixture of an appropriate carbohydrate (or polyol) with pyridine or triethylamine (at the ratio 1 : 3) dissolved in dioxane was slowly added dropwise at strirring three-fold molar amount of phosphorylating agent in the same solvent. The reaction progress was monitored by ^{31}P NMR spectroscopy and TLC. When reaction was completed, the mixture was stirred for 1 h at room temperature, then filtered, and the solvent was removed in a vacuum. The residue was dissolved in benzene, sulfur in 10% excess was added, the mixture was stirred for 2 h and left overnight. If the reaction was not completed, then the mixture was heated to 100°C for 30 min. Solvent was removed in a vacuum, the residue was subjected to column chromatography eluting consecutively with benzene and system B. Isolated products were dried in a vacuum.

1,2,4-Tris-(2'-thio-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)butanetriol (XX). From 1.0 g of 1,2,4-butanetriol, 4.8 g of neopentylenechlorophosphite and 0.9 g of sulfur was obtained 0.64 g of product **XX**. White crystalline substance. R_f 0.51 (B). ^{1}H NMR spectrum ($CDCl_3$, δ, ppm): 0.95 s, 1.22 s (18H, $OCH_2(CH_3)_2CH_2O$), 2.15 d (2H, $^2J_{HH}$ 6.05 Hz), 3.92 m (6H^e, $OCH_2C(CH_3)_2$, $^2J_{HH}$ 11.9 Hz), 3.94 m (2H, $^2J_{HH}$ 6.5 Hz, $^3J_{HP}$ 10.5 Hz), 4.10 m (6H^a, $OCH_2C\cdot(CH_3)_2$, *J* 6.2 Hz, $^2J_{H^aH^e}$ 10.9 Hz), 4.28 d (2H, $^2J_{1H2H}$ 4.3 Hz, $J_{H^aH^e}$ 3.4 Hz), 4.38 m (1H, $^3J_{2H3H}$ 10.4 Hz). Found, %: C 38.15; H 6.26; P 15.49; $C_{19}H_{37}O_9P_3S_3$. Calculated, %: C 38.12; H 6.23; P 15.52. *M* 598.62. Found, *M* (^{12}C): 598.86. Calculated, *M* (^{12}C): 598.43.

2,3,4-Tris-(2'-thio-1',3',2'-dioxaphosphorinane)-methyl-β-*D*-xylopyranoside (XXI). From 1.0 g of methyl-β-*D*-xylopyranoside, 2.5 g of propylenechlorophosphite and 0.5 g of sulfur was obtained 1.02 g of product **XXI**. White crystalline substance. R_f 0.6 (B). ^{1}H NMR spectrum ($CDCl_3$, δ, ppm): 1.72, 1.73, 1.77 m (3H^e, OCH_2CH_2, $^2J_{HH}$ 10.8 Hz), 2.27, 2.32, 2.35 m (3H^a, OCH_2CH_2, ^2J 6.1 Hz, $^2J_{H^aH^e}$ 10.7 Hz), 3.52 s (3H, OCH_3), 3.92 m (2H, $^2J_{HH}$ 6.4 Hz, $^3J_{HP}$ 10.2 Hz), 4.31, 4.36, 4.50 m (6H^e, OCH_2CH_2), 4.26 d (2H, $^2J_{1H2H}$ 4.1 Hz), 4.36 m (1H, $^3J_{2H3H}$ 10.3 Hz), 4.60 d (1H, ^3J 3.4 Hz), 4.58, 4.64, 4.70 m (6H^a, OCH_2CH_2, $^2J_{H^aH^e}$ 10.5 Hz), 4.97 d (1H, $^3J3_{H4H}$ 3.4 Hz). Found, %: C 31.51; H 4.80; P 16.28; $C_{15}H_{27}O_{11}P_3S_3$. Calculated, %: C 31.47; H 4.75; P 16.23.

2,3,4-Tris--(2'-thio-5',5'-dimethyl-1',3',2'-dioxaphosphorinane)methyl-β-*D*-xylopyranoside (XXII). From 1.0 g of methyl-β-*D*-xylopyranoside, 3.0 g of neopentylenechlorophosphite and 0.6 g of sulfur was obtained 0.92 g of product **XXII**. White crystalline substance. R_f 0.51 (B). ^{1}H NMR spectrum ($CDCl_3$, δ, ppm): 0.86 s, 1.24 s [18H, $OCH_2(CH_3)_2CH_2O$], 2.15 d (2H, $^2J_{HH}$ 6.05 Hz), 3.92 m [6H^e, $OCH_2C(CH_3)_2$, $^2J_{HH}$ 11.9 Hz], 3.94 m (2H, $^2J_{HH}$ 6.5 Hz, $^3J_{HP}$ 10.5 Hz), 4.10 m (6H^a, $OCH_2C(CH_3)_2$, *J* 6.2 Hz, $^2J_{H^aH^e}$ 10.9 Hz), 4.28 d (2H, $^2J1_H2_H$ 4.3 Hz, $J_{H^aH^e}$ 3.4 Hz), 4.38 m (1H, $^3J_{2H3H}$

10.4 Hz). Found, %: C 30.43; H 5.96; P 14.10; $C_{21}H_{39}O_{11}P_3S_3$. Calculated, %: C 30.41; H 5.99; P 14.15. *M* 656.65. Found, *M* (^{12}C): 655.70. Calculated, *M* (^{12}C): 656.44.

3,5,6-Tris-(2'-thio-5',5'-dimethyl-1',3',2'-dioxaphos-phorinane)-1,2-*O*-isopropylidene-*D*-glucofuranoses (XXIII). From 1.0 g of 1,2-*O*-isopropylidene-glucofuranose, 2.3 g of neopentylenechlorophosphite and 0.6 g of sulfur was obtained 1.04 g of thiophosphate (**XXIII**). White crystalline substance. R_f 0.69 (B). ^1H NMR spectrum ($CDCl_3$, δ, ppm): 0.93 s, 1.25 s [18H, $OCH_2(CH_3)_2CH_2O$], 3.49 s (3H, OCH_3), 3.84 m [6H^e, $^2J_{H^aH^e}$ 5.1 Hz $OCH_2C(CH_3)CH_2O$], 3.91 m (1H^e, $^3J_{6H6H}$ 9.5 Hz, $^3J_{HP}$ 4.1 Hz), 3.98 m (1H, $^3J_{HP} \leq 1$ Hz), 4.24 m (1H^a, $^3J_{6H6H}$ 9.5 Hz), 4.31 d (1H, $^3J_{4H5H}$ 4.6 Hz), 4.37 m [6H^a, $^2J_{H^aH^e}$ 5.1 Hz $OCH_2C(CH_3)CH_2O$], 4.58 d (1H, $^3J_{1H2H}$ 3.6 Hz), 4.91 m (1H, $^3J_{4H5H}$4.6 Hz, $^3J_{HP}$ 12.8 Hz), 5.91 d (1H, $^3J_{1H2H}$ 3.6 Hz). Found, %: C 40.51; H 5.90; P 13.01; $C_{24}H_{43}O_{12}P_3S_3$. Calculated, %: C 40.44; H 6.08; P 13.03.

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