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New Type Phosphorous Amides Derived from Protected Monosaccharides

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Abstract — Three synthetic routes to hydrogen phosphoramidites derived from protected hydrocarbons containing one free secondary hydroxy group are explored: phosphorylation with (diethylamido)phosphorous dichloride, acidolysis of tetraalkyldiamides derived from sugars, and phosphorylation with phosphorous tetraalkyldiamides. The last route was found to be preferred. Some properties of the prepared dialkylamidoglycophosphites were studied: stability, phosphorylating activity, and behavior in oxidation reactions.
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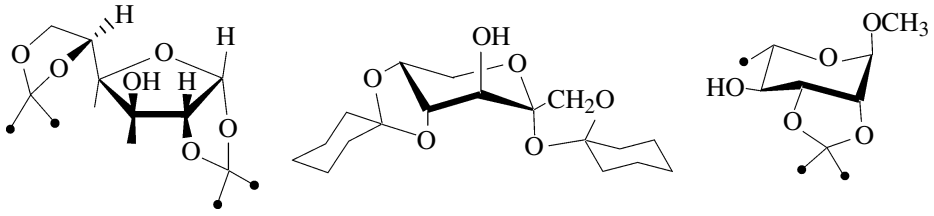
Organic derivatives of phosphorous acid belong to the most important objects for study in organophosphorus chemistry. These compounds are widely used for solving various problems of fine organic synthesis, including synthesis of phosphorus-containing natural compounds and their analogs [1, 2]. Among the phosphorylating agents actively used over the past 15–20 years, trivalent phosphorus amides merit notice.

Hydrogen phosphoramidites, including those derived from carbohydrates, have been scarcely studied. At the same time, such compounds present much interest as intermediates in the synthesis of earlier unknown carbohydrate structures possessing a P–N bond, and as ligands for potential metal-complex catalysts.

The present work was focused on searching for convenient synthetic routes of hydrophosphoryl compounds derived from phosphorous amides and sugars. As objects for study we took monosaccharides with one free secondary hydroxy group, viz. 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (diacetone glucose) (**I**), 1,2:4,5-*O*-cyclohexylidene-α-D-fructopyranose (**II**), and 2,3-*O*-isopropylidene-α-L-methylraminopyranoside (**III**).

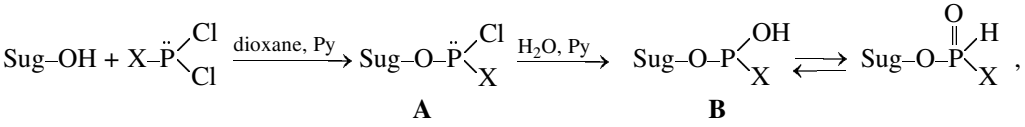


I **II** **III**

The synthesis of monosaccharide acid amides was performed by two procedures: indirect and direct. In the first case, carbohydrates were phosphorylated with phosphorous acid derivatives containing no hydrophosphoryl function. The direct synthesis involved phosphorylation with phosphorous diamides that already possessed the desired group.

In the indirect synthesis, we used two approaches: reaction of sugar with (diethylamido)phosphorous dichloride and acidolysis of carbohydrate-containing phosphorous diamides.

Earlier we showed [3] that hydrophosphoryl derivatives of monosaccharides are easily formed by the reactions of monosaccharides with phosphorous and phosphonous dichlorides by following scheme:

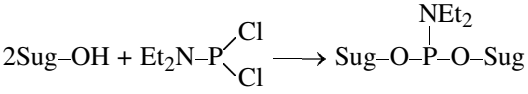


A **B**

X = OR, Ph.

The ^{31}P NMR spectra of the reaction mixture gave evidence for the formation of monochlorides **A** (δ_P 168–172 ppm). In the final step we performed hydrolysis leading to desired hydrophosphoryl compounds **B**.

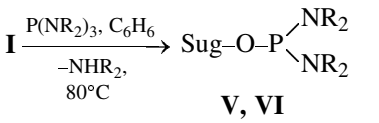
Further we involved in this reaction phosphorylating agents containing a P–N bond, viz. (diethylamido)-phosphorous dichloride. In this case, symmetrical amidodiester **IV** formed rather than hydrophosphoryl carbohydrate derivatives:



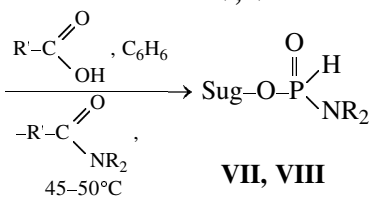
I **IV**

Compound **IV** proved to be fairly stable, and we could isolate it and examine its structure by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy to find that it is similar to the structure of the related compound prepared earlier from diacetone glucose and hexaethylphosphorous triamide [4]. With a twofold excess of (diethylamido)-phosphorous dichloride, we observed formation of symmetrical amidodiester **IV**.

The second indirect synthetic approach involved acidolysis of phosphorous diamides. Diamides **V** and **VI** were prepared by heating equimolar amounts of sugar **I** and hexaalkylphosphorous triamide:



V, VI

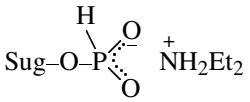


VII, VIII

R = Me (**V**), Et (**VI**); R' = H_2C=CH, F_3C.

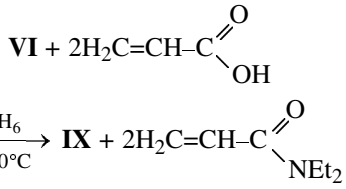
The ^{31}P NMR spectra of the reaction mixture contained signals at δ_P ~15 and ~17 ppm ($^1J_{PH}$ ~656 and ~632 Hz) from compound **VII**. The acidolysis proceeded mush slower than with alkyl phosphorodiamidites [5]. We explain this result by steric hindrances created by the isopropylidene protecting groups that shield the phosphorus atom. The slow course of this reaction led to by-product formation. In view of the fact that carboxylic acids can attack both the phosphamide center and the C–O bond of the acetal protective groups, we can suggest that part of sugar molecules might have lost the protective groups in the acidic medium. Evidence for this suggestion was provided by the detection by TLC of phosphorus-free sugar molecules, viz. monoacetone glucose and free glucose.

Furthermore, hydrogen phosphoramidites **VII** and **VIII** are fairly readily hydrolyzed to form glycophosphorous acid. Thus the reaction of diamide **VI** with acetic acid gave diethylammonium salt **IX** as the major product. This compound was isolated by column chromatography.



IX

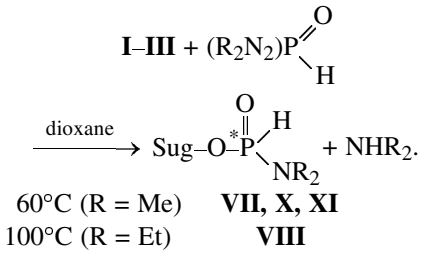
We also prepared compound **IX** by adding two equiv of acrylic acid to tetraethyldiamide **VI**:



In the ^{31}P NMR spectrum of the reaction mixture we observed one doublet signal near δ_P 1.0 ppm ($^1J_{PH}$ 627.7 Hz). The yields of compound **IX** were low in both cases (ca. 7%), which is probably explained by the low selectivity of this reaction, resulting in partial removal of the acetal protective groups. The structure of compound **IX** was elucidated by ^{1}H and ^{31}P NMR spectroscopy and confirmed by elemental analysis. Spectral characteristics of compound **IX** obtained by acidolysis with acetic or acrylic acid are identical.

The direct synthesis makes use of phosphorous tetraalkyldiamides which are quite available [6].

With phosphorous tetramethyldiamide, the reaction proceeded almost quantitatively. After 1.5 h in the ^{31}P NMR spectrum of the reaction mixture were regis-

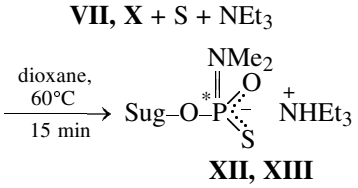


tered two doublets at δ_P ~15 and 18 ppm ($^1J_{PH}$ 630 and 650 Hz), corresponding to two diastereomers.

Phosphorylation with phosphorous tetraethyldiamide proceeded less actively. Refluxing in dioxane for 4 days was required; therewith, by-product formation was observed.

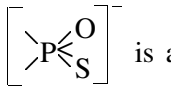
Compounds **VII**, **VIII**, **X**, and **XI** were isolated by column chromatography. In the individual state, they are unstable and decompose with time. In solution the decomposition is slower, which allowed us to measure the ^{13}C NMR spectrum of fructopyranose derivative **X**. The spectrum contained signals characteristic of the sugar frame and two doublets at δ_P 33.9 and 34.3 ppm ($^2J_{PC}$ 6.7 Hz) characteristic of the dimethylamido group.

We also studied some reactions of the obtained monosaccharide hydrophosphoryl derivatives containing a P–N bond. Oxidation with sulfur in the presence of equimolar amount of triethylamine gave thionophosphate salts **XII** and **XIII**:

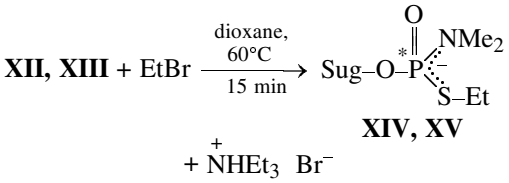


The reaction proceeded quantitatively. The ^{31}P NMR spectrum of the reaction mixture displayed two singlets at δ_P 66 and 67 ppm. Crude compounds **XII** and **XIII** are thick bright yellow syrups.

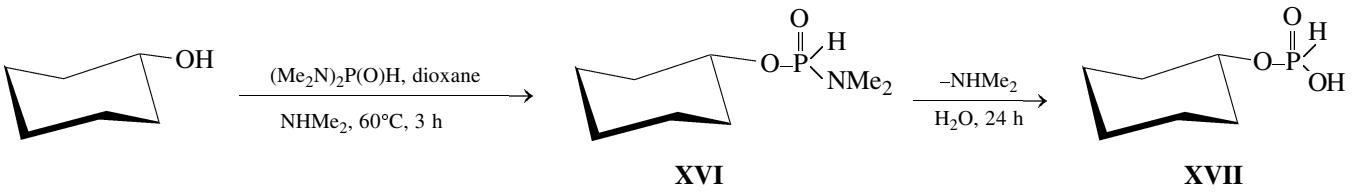
Compounds **XII** and **XIII** without isolation were reacted with ethyl bromide.

As known,  is an ambident ion and can

be alkylated by either the sulfur or oxygen atom. According to [7], alkylation by sulfur is preferred. In the case of glucose derivative **XII**, we detected in the ^{31}P NMR spectrum of the reaction mixture both S- and O-alkylation products: singlets at δ_P 74.5 (thionophosphate) and 36.5 and 37.9 ppm (thiolophosphate). From the integral intensities of the corresponding signals, the ratio of the products was estimated at 4.7 : 6.7. With fructose derivative **XIII**, the reaction proceeded more smoothly, and the ^{31}P NMR spectrum of the reaction mixture showed signals of the S-alkylation product only (δ_P 36.4 and 36.8 ppm).



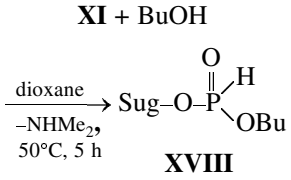
Further we studied the phosphorylating ability of the hydrogen tetramethylphosphorodiamidites. To confirm our suggestion that hydrogen phosphoramidites are sensitive to hydrolysis, we performed a model experiment with cyclohexanol:



The reaction was performed at 60°C for 3 h. The ^{31}P NMR spectra of the reaction mixture contained a doublet at δ_P 12.4 ppm ($^1J_{PH}$ 628.0 Hz) assignable to amide **XVI**. It was treated *in situ* with equimolar amount of water. After 24 h, in the ^{31}P NMR spectrum we observed only one signal at δ_P 4.6 ppm ($^1J_{PH}$ 680.7 Hz), corresponding to cyclohexyl phosphite **XVII**.

Amide **XI** was brought in alcoholysis with butanol.

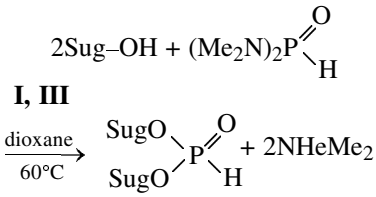
Compound **XVIII** was purified by column chromatography and obtained as a labile yellowish oil. Its



XVIII

structure was proved by ^{31}P and ^{13}C NMR spectroscopy, and the composition was determined by elemental analysis. It is significant that phosphite **XVIII** was obtained with a high optical yield (75% of the major diastereomer).

As the next step, we took monosaccharides **I** and **III** as the alcohol components. The reaction was performed in dioxane by mixing 2 equiv of saccharide with 1 equiv of tetramethylphosphorodiamidite:



XIX, XX

With a slight excess of phosphorylating agent (1.3 equiv per 1 equiv of carbohydrate), the reaction proceeds in reasonable yield. In the case of diacetone glucose (**I**), we failed to bring the reaction to completion, probably, due to steric hindrances. The only free 4-OH group in ramnopyranoside **III** is sterically more accessible; as a result, the yield of the corresponding glycophosphite is higher. In the ^{31}P NMR spectrum, the signals of phosphites **XIX** and **XX** are doublets of doublets (δ_P ~7 ppm, $^1J_{PH}$ ~715 Hz, $^2J_{PH}$ ~10 Hz). The structures of the products were proved by ^1H NMR and the compositions were determined by elemental analysis.

Thus, carbohydrate phosphoramidites are best prepared by the direct synthesis with use of phosphorous tetraalkyldiamides. The availability of these starting materials opens up the way to their wide use in fine organic synthesis. The hydrogen phosphoramidites containing a carbohydrate residue can be used as intermediates in synthetic practice and offer possibilities for preparing a broad range of P(V) amides and esters that are interesting as bioregulators.

EXPERIMENTAL

The ^1H NMR spectra were registered on a Bruker WM-250 instrument (250 MHz). The ^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer (50.32 MHz). The ^{31}P NMR spectra were measured on a Bruker WP-80SY instrument (32.4 MHz) against external 85% phosphoric acid. Column chromatography was performed on Silica gel L 100/160. TLC analysis was performed on Silufol UV-254 plates using the following systems: hexane-dioxane, 5 : 1 (A), hexane-dioxane, 7 : 1 (B), benzene-dioxane, 7 : 1 (C), benzene-dioxane, 8 : 1 (D), benzene-dioxane, 10 : 1 (E), and benzene-dioxane, 12 : 1 (F); development in iodine vapor and by calcination.

All syntheses were performed in dry solvents under dry and oxygen-free argon.

Bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3'-(diethylphosphoramidite) (IV). To a solution of 0.75 g (0.0043 mol, 1.1 equiv) of (diethylamido)phosphorous dichloride in 3 ml of dioxane, a mixture of 1.02 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and 0.77 g of pyridine in 5 ml of dioxane was added at 12°C (bath temperature). The mixture was stirred for 30 min at room temperature and cooled, after which a solution of 0.08 g of water in 3 ml of dioxane was added. Stirring was continued for 30 min at room temperature, the pyridine hydrochloride precipitate was filtered off, and the filtrate was evaporated. The residue was quickly transferred to a silica gel column and eluted with system E. Yield 0.18 g (15%) of compound **IV**, yellowish oil, R_f 0.6 (A), $[\alpha]_D^{20}$ –400 (c = 1, CH_2Cl_2). ^1H NMR spectrum (C_6D_6), δ, ppm: 1.0 t (6H, $2NCH_2CH_3$), 1.1–1.5 s [24H, $4(C(CH_3)_2)$]; 3.01, 3.02 m (4H, $2NCH_2CH_3$, $^3J_{PH}$ 10.3 Hz); 4.12 d.d (2H, $H^{6'}$, $^2J_{H^{6'}H^6}$ 8.7 Hz, $^3J_{H^{6'}H^5}$ 5.6 Hz); 4.16 d.d (2H, H^6, $^3J_{H^6H^{6'}}$ 8.7 Hz, $^3J_{H^6H^5}$ 3.9 Hz); 4.5 d.d.d (2H, H^5, $^3J_{H^5H^6}$ 3.9 Hz, $^3J_{H^5H^{6'}}$ 5.6 Hz, $^3J_{H^5H^4} < 1$ Hz), 4.5 d.d (2H, H^4, $^2J_{H^4H^3}$ 3.3 Hz, $^3J_{H^4H^5} < 2$ Hz); 4.8 d.d.d (2H, H^3, $^3J_{H^3H^2}$ was not determined due to overlap of signals, $^3J_{H^3H^4}$ = 3.3 Hz, $^2J_{PH}$ = 10.2 Hz); 4.64, 4.84 d.d (2H, H^2, $^3J_{H^2H^3}$ was not determined due to overlap of signals, $^3J_{H^2H^1}$ 3.8 Hz); 5.94, 5.96 (d, 2H, H^1, $^3J_{H^1H^2}$ 3.8 Hz). ^{31}P NMR spectrum (C_6H_6), δ, ppm: 144.7 s. Found, %: C 54.01; H 2.15; P 4.79. $C_{28}H_{48}NO_{12}P$. Calculated, %: C 53.98; H 2.28; P 4.75.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose 3-(diethylammonium phosphite) (IX). *a*. To a solution of 1.49 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-(tetraethylphosphorodiamidite), 0.23 g of acetic acid was added. The reaction mixture was stirred at room temperature for 2 h, left to stand for 2 h, and then subjected to column chromatography, eluent C. Yield 0.08 g (6%).

b. To a solution of 1.30 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-(tetraethylphosphorodi-

amidite) in 4 ml of benzene, a solution of 0.43 g of acrylic acid in 2 ml of benzene was slowly added dropwise at 15°C (bath temperature). The reaction mixture was stirred at room temperature for 30 min then heated at 45–50°C for 10 h. The solvent was evaporated, and the residue was purified by column chromatography, eluent C. Yield 0.1 g (8.4%), colorless oil, R_f 0.30 (C). ^{31}P NMR spectrum ($CHCl_3$), δ, ppm: 1.0 d ($^1J_{PH}$ 630.2 Hz). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.0 t (6H, $2NCH_2CH_3$), 1.1–1.7 s [24H, $4(C(CH_3)_2)$], 2.7 m (4H, $2NCH_2CH_3$), 3.8 d.d (1H, $H^{6'}$, $^2J_{H^{6'}H^6}$ 8.5 Hz, $^3J_{H^{6'}H^5}$ 8.5 Hz); 3.9 d.d (1H, H^6, $^3J_{H^6H^{6'}}$ 8.5 Hz, $^3J_{H^6H^5}$ 3.9 Hz), 3.9 m (2H, H^5, H^4, the coupling constant was not determined due to overlap of signals), 4.1 m (1H, H^3, $^2J_{PH}$ 10.7 Hz); 4.5 d.d (1H, H^2, $^3J_{H^2H^3}$ was not determined due to overlap of signals, $^3J_{H^2H^1}$ 3.7 Hz), 5.6 d (1H, H^1, $^3J_{H^1H^2}$ 3.7 Hz), 6.7 d (1H, PH, $^1J_{PH}$ 630.2 Hz), 9.1 br.s (2H, NH). Found, %: C 48.74; P 7.63. $C_{16}H_{32}NO_8P$. Calculated, %: C 48.36; P 7.79.

Monosaccharide hydrogen dimethylphosphoramidites VII, X, and XI *(general procedure).* To 1.0 equiv of monosaccharide dissolved in 5 ml of dioxane, 1.3 equiv of phosphorous tetramethyldiamide was added. The mixture was heated at 60°C for 1.5 h.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose 3-(hydrogen dimethylphosphoramidite) (VII) was prepared from from 0.78 g of 5,6-di-*O*-isopropylidene-α-D-glucofuranose and 0.53 g of phosphorous tetramethyldiamide and purified by column chromatography, eluent C. Yield 0.29 g (28%), colorless . R_f 0.23 (B). ^{31}P NMR spectrum ($CHCl_3$), δ, ppm: 16.8, 19.3 (d, $^1J_{PH}$ = 655.7 Hz, $^1J_{PH}$ = 631.6 Hz).

1,2:4,5-Di-*O*-cyclohexylidene-α-D-fructopyranose 3-(hydrogen dimethylphosphoramidite) (X) was prepared from 0.72 g of 1,2:4,5-di-*O*-cyclohexylidene-α-D-fructopyranose and 0.38 g of phosphorous tetramethyldiamide and purified by column chromatography, eluent F. Yield 0.23 g (25%), colorless oil, R_f 0.21 (E). ^{31}P NMR spectrum ($CHCl_3$), δ, ppm: 16.3, 19.3 (d, $^1J_{PH}$ 654.1). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 23.7–25.0 s (cyclohexylidene protection), 33.9, 34.3 d (N–CH_3, $^2J_{PC}$ 6.6 Hz), 35.3–37.8 s (cyclohexylidene protection), 77.1, 71.2 s (C^1), 72.1, 72.3 d (C^4, $^3J_{PC}$ 7.9 Hz, $^3J_{PC}$ 5.5 Hz), 73.1, 73.2 s (C^5), 75.4 d (C^3), $^2J_{PC}$ < 2 Hz), 103.5 d, 104.1 d (C^2, $^3J_{PC}$ 4.0 Hz, $^3J_{PC}$ 4.9 Hz), 108.7,112.5, and 110.4, 112.8 s (C_{quat}). Found, %: C 53.99; H 7.99. $C_{20}H_{34}NO_7P$. Calculated, %: C 55.67; H 7.94.

2,3-*O*-Isopropylidene-α-L-methylramnopyranoside 4-(hydrogen dimethylphosphoramidite) (XI) was prepared from 0.62 g of 2,3-*O*-isopropylidene-α-L-methylramnopyranoside and 0.50 g of phosphorous tetramethyldiamide and purified by column chromatography, eluent D. Yield 0.18 g (21%), colorless oil, R_f 0.22 (D). ^{31}P NMR spectrum ($CHCl_3$), δ, ppm: 15.8, 18.9 d ($^1J_{PH}$ 645.3 Hz, $^1J_{PH}$ 658.2 Hz).

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose 3-(hydrogen diethylphosphoramidite) (VIII). To a solution of 0.55 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose in 5 ml of dioxane, 0.61 g of phosphorous tetraethyldiamide was added. The mixture was refluxed in dioxane for four days, then the solvent was evaporated, and the residue was purified by column chromatography, eluent B. Yield 0.13 g (15%), colorless oil, R_f 0.22 (B). ^{31}P NMR spectrum ($CHCl_3$), δ, ppm: 14.8, 18.1 d ($^1J_{PH}$ 657.6 Hz, $^1J_{PH}$ 618.5 Hz).

Monosaccharide (*S*-ethyl dimethylphosphoramidothioates) XIV and XV. To 1.0 equiv of monosaccharide hydrogen dimethylphosphoramidite in 5 ml of dioxane, 1.2 equiv of sulfur and 1.2 equiv of triethylamine were added. The mixture was heated at 60°C until sulfur dissolved completely and cooled, after which 1.2 equiv of ethyl bromide was added, and the mixture was heated again to 60°C for 15 min until triethylamine hydrobromide began to precipitate. The precipitate was filtered off, the filtrate was evaporated, and the residue was purified by column chromatography.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose 3-(*S*-ethyl dimethylphosphoramidothioate) (XIV) was prepared from 1.23 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-(hydrogen dimethylphosphoramidite), 0.13 g of sulfur, 0.43 g of triethylamine, and 0.46 g of ethyl bromide and purified by column chromatography, eluent A. Yield 0.29 g (20%), yellow oil, R_f 0.2 (A). ^{31}P NMR spectrum ($CHCl_3$), δ, ppm: 36.5, 37.9 s. ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.0 s (SCH_2CH_3), 16.36 d (SCH_2CH_3, $^2J_{PC}$ 6.4 Hz), 22.6–26.7 s ($C(CH_3)_2$), 36.4 d (NCH_3, $^2J_{PC}$ 3.5 Hz), 67.4 s (C^6), 72.2 s (C^5), 78.9 d (C^3, $^2J_{PC}$ 5.5 Hz), 80.7 d (C^4, $^3J_{PC}$ 8.9 Hz), 83.4 s (C^2), 105.1 s (C^1), 109.1, 112.2 s ($C(CH_3)_2$). Found, %: C 45.93; H 7.11, P 7.35. $C_{16}H_{30}NO_7PS$. Calculated, %: C 46.71; H 7.35; P 7.53.

1,2:4,5-Di-*O*-cyclohexylidene-α-D-fructopyranose 3-(*S*-ethyl dimethylphosphoramidothioate) (XV) was prepared from 1.34 g of 1,2:4,5-di-*O*-cyclohexylidene-α-D-fructopyranose 3-(hydrogen dimethylphosphoramidite), 0.12 g of sulfur, 0.37 g of triethylamine, and 0.40 g of ethyl bromide and purified by column chromatography, eluent E. Yield 0.72 g (47.5%), yellow oil, R_f 0.60 (E). ^{31}P NMR spectrum

($CHCl_3$), δ, ppm: 37.3, 37.7 s. ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.7 s (SCH_2CH_3), 23.4 d ($SCH_2 \cdot CH_3$, $^2J_{PC}$ < 2 Hz), 23.2–24.5, 34.9–36.2 s (cyclohexylidene protections), 37.3 d (NCH_3, $^2J_{PC}$ 6.8 Hz), 59.9 s (C^6), 71.0 s (C^1), 73.0 d (C^4, $^3J_{PC}$ < 2 Hz), 74.9 s (C^5), 77.1 d (C^3, $^2J_{PC}$ 9.8 Hz), 103.0 d (C^2, $^3J_{PC}$ < 2 Hz), 109.5 s and 111.9 s (C_{quat}). Found, %: C 53.90; H 7.50, P 6.10. $C_{22}H_{38}NO_7PS$. Calculated, %: C 53.75; H 7.79; P 6.30.

Cyclohexyl phosphite (XVII). To a solution of 0.59 g of cyclohexanol in 3 ml of dioxane, 1.04 g of phosphorous tetramethyldiamide was added. The mixture was heated at 60°C for 3 h and cooled to room temperature. Water, 0.11 g, in 2 ml of dioxane was added, and the mixture was left for 24 h. The solvent was evaporated, and the residue was subjected to column chromatography, eluent A, R_f 0.15 (A). ^{31}P NMR spectrum ($CHCl_3$), δ, ppm: 4.6 d ($^1J_{PH}$ 680.7 Hz). ^1H NMR spectrum (C_6D_6) , δ, ppm: 1.0 m (2H, H^4), 1.5 m (2H, H^3), 1.8 m (2H, H^2), 3.9 br.s (1H, POH), 4.4 d.d (1H, H^1, $^2J_{PH}$ 15.3 Hz, $^3J_{H^1H^2}$ 7.3 Hz), 6.9 d (1H, PH, $^1J_{PH}$ 680.7 Hz). Found, %: C 44.15; P 18.60. $C_6H_{13}O_3P$. Calculated, %: C 43.90; P 18.87.

2,3-*O*-Isopropylidene-α-L-methylramnopyranoside 4-(butyl phosphite) (XVIII). To a solution of 0.93 g of compound **XI** in 5 ml of dioxane, 0.24 g of butanol was added. The mixture was heated for 5 at 50°C, the solvent was evaporated, and the residue was purified by column chromatography, eluent A. Yield 0.20 g (20.1%), mobile yellow oil, R_f 0.53 (A). ^{31}P NMR spectrum ($CHCl_3$), δ, ppm: 6.93 d, 8.04 d ($^1J_{PH}$ 683.5 Hz, $^1J_{PH}$ 692.6 Hz). ^{13}C NMR spectrum (C_6D_6), δ, ppm: 14.1 s ($OCH_2CH_2CH_2CH_3$), 17.8 s ($OCH_2CH_2CH_2CH_3$), 19.4 s (C^6), 27.0 s and 28.5 s ($C(CH_3)_2$), 33.1 d ($OCH_2CH_2CH_2CH_3$, $^3J_{PC}$ 5.8 Hz), 55.0 s (OCH_3), 64.8 d ($OCH_2CH_2CH_2CH_3$, $^2J_{PC}$ 9.6 Hz), 65.6 d (C^5, $^3J_{PC}$ 5.3 Hz) 77.2 s (C^2), 77.7 d (C^3, $^3J_{PC}$ 5.3 Hz), 79.6 d (C^4, $^2J_{PC}$ 8.4 Hz), 98.7 s (C^1), 110.3 s and 110.7 s ($C(CH_3)_2$). Found, %: C 46.8; P 9.83. $C_{14}H_{27}O_7P$. Calculated, %: C 49.7; P 9.15.

Diglycophosphites XIX and XX *(general procedure).* To a solution of 2 equiv of monosaccharide in 3 ml of dioxane, 1.3 equiv of phosphorous tetramethyldiamide was added. The mixture was heated for 6 h at 60°C, the solvent was evaporated, and the residue was purified by column chromatography.

Bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3'-phosphite (XIX) was prepared from 0.94 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and 0.32 g of phosphorous tetramethyldiamide and purified by column chromatography, eluent D. Yield 0.25 g (12%), colorless oil, R_f 0.41 (D). ^{31}P NMR spectrum (C_6H_6), δ, ppm: 7.1 d.d ($^1J_{PH}$ 721.1 Hz, $^2J_{PH}$ 10.1 Hz). ^1H NMR spectrum (C_6D_6), δ, ppm: 1.05–1.34 s (24H, $4C(CH_3)_2$), 4.0 m (4H, H^4, $H^{6'}$, the coupling constant was not determined due to overlap of signals), 4.3 m (4H, H^5, H^6, the coupling constant was not determined due to overlap of signals), 4.8 d.d (2H, H^2, $^3J_{H^2H^1}$ 3.4 Hz, $^3J_{H^2H^3}$ was not determined due to overlap of signals), 5.2 d (2H, H^3, $^2J_{H^3P}$ 10.1 Hz), 5.8, 5.9 d (2H, $^3J_{H^1H^2}$ 3.4 Hz), 7.0 d (1H, PH, $^1J_{PH}$ 721.1 Hz). Found, %: C 50.30; P 4.91. $C_{24}H_{39}O_{13}P$. Calculated, %: C 50.88; P 5.47.

Bis(2,3-*O*-isopropylidene-α-L-methylramnopyranoside) 4,4'-phosphite (XX) was prepared 1.11 g of 2,3-*O*-isopropylidene-α-L-methylramnopyranoside and 0.44 g of phoshorous tetramethyldiamide and purified by column chromatography, system E. Colorless oily substance. Yield 0.60 g (24%), colorless oil, R_f 0.37 (E). ^{31}P NMR spectrum (C_6H_6), δ, ppm: 7.1 d.d ($^1J_{PH}$ 713.8 Hz, $^2J_{PH}$ 10.5 Hz). ^1H NMR spectrum (C_6D_6), δ, ppm: 1.2 s (6H, $2C^6H_3$); 1.4–1.6 (s, 12H, $2C(CH_3)_2$); 3.03, 3.05 s (6H, $2OCH_3$); 3.7 m (2H, H^5, the coupling constant was not determined due to overlap of signals), 4.1 d.d (2H, H^3, $^3J_{H^3H^2}$ 5.5 Hz, $^3J_{H^3H^4}$ 4.3 Hz), 4.2 d.d (2H, H^2, $^3J_{H^2H^1}$ 6.1 Hz, $^3J_{H^2H^3}$ 5.5 Hz), 4.4 m (2H, H^4, $^2J_{H^4P}$ 10.5 Hz, $^3J_{H^4H^5}$ 7.3 Hz, $^3J_{H^4H^3}$ 4.3 Hz), 4.8 d (2H, H^1, $^3J_{H^1H^2}$ 6.1 Hz), 7.4 d (1H, PH, $^1J_{PH}$ 713.8 Hz). Found, %: C 51.0; P 6.91. $C_{20}H_{35}O_{11}P$. Calculated, %: C 49.79; P 6.42.

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