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Reaction of Acetyl- and Alkylideneglycosylamines with Diphenylphosphinous Acid

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Abstract — An original method of synthesis of optically active α-aminophosphoryl compounds containing a carbohydrate residue is proposed.
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The Kabachnik–Fields reaction discovered in 1952 still remains an effective method of phosphorus–carbon bond formation [1]. Despite the long-standing researcher's interest in methods of synthesis and properties of α-aminophosphoryl compounds, a lot of problems in this field of organophosphorus chemistry have still to be solved. Possibilities for modification aimed at obtaining α-aminophosphoryl compounds on the basis of new substrates, first of all of natural origin, are far from being exhausted. Development of new convenient procedures for synthesis of such derivatives under mild conditions and in high yields still remains an urgent problem. It is noteworthy glycosylamines have never been introduced in the Kabachnik–Fields reaction. At the same time, mutarotation of these compounds involves intermediate formation of the imino form which is expected to react with hydrophosphoryl compounds.

We have studied the reaction of unprotected mono- and disaccharide anilides with dipenylphosphinous acid. It has been shown that the phosphorus-containing function adds to the glycoside center to form α-amino-*tert*-phosphine oxides. The process is complicated by furanization of the carbohydrate fragment [2]. However, provided the carbohydrate fragment has been preserved, the reaction leads to α-aminophosphoryl derivatives of carbohydrates, which represent a wide and chemically diverse class of compounds. Some of such compounds possess important and useful properties, e.g., exhibit high and diverse physiological activity [3–5]. Therefore, we extended investigations in this area and turned to phosphorylation of anilines derived from protected monosaccharides. Here we present the first results of this research.

As substrates for phosphorylation we chose accessible triose, pentose, and hexose amino derivatives representing both open-chain and cyclic (pyranose and furanose) monosaccharides. Full protection of hydroxy groups in the carbohydrate fragment of the anilide molecules excluded their furanization. Throughout the investigation the nitrogen-containing part of the anilines and phosphorylating agent were not varied. Such set of *N*-glycosides allowed us to study the reactivity of the anilines in the non-classical variant of the Kabachnik–Fields reaction as a function of the structure of their carbohydrate moiety and to draw tentative conclusions of the reaction scheme.

As the simplest carbohydrate-containing azomethine we used *N*-[(2,2-dimethyl-1,3-dioxolan-4-yl)methylene]aniline (**II**). Its synthesis has been described by Yoshimura et al. [6] who found that this compound is unreasonable to isolate by distillation or crystallization because the conversion of the imino to amino form. Therefore, we applied compound **II** without isolation. Its formation was detected by TLC, after which the compound was immediately involved into the phosphorylation reaction. Glycerose **I** was synthesized alongside the procedure in [7].

We found that reaction of compound **II** with dipenylphosphinous acid (**III**) proceeds under fairly mild conditions (at 20°C) and is complete in 2–3 h.

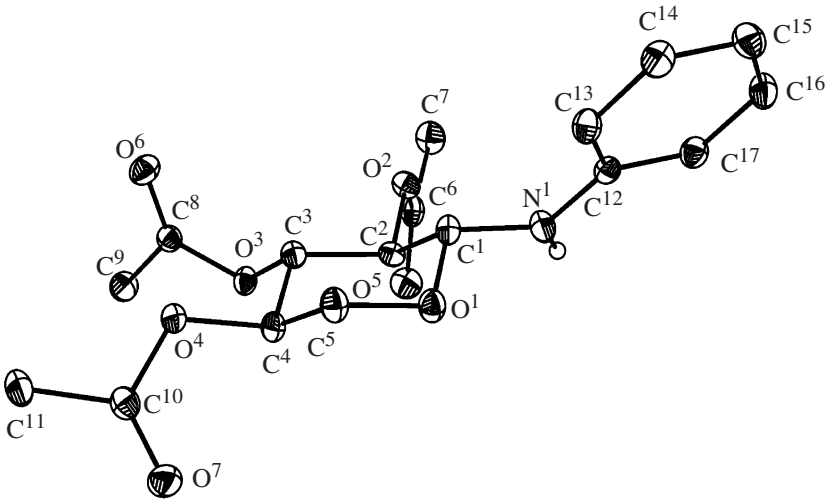
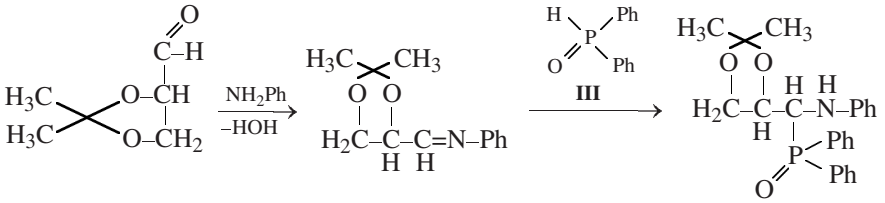


Fig. 1. General view of molecule **V** with thermal ellipsoids drawn at the 50% probability level. Bond lengths (Å): O^1–C^1 1.452(2), O^1–C^5 1.422(2), N^1–C^{12} 1.392(2), N^1–C^1 1.412(2), O^2–C^2 1.436(2), C^3–O^3 1.438(2), C^4–O^4 1.437(2), and O^5–C^6 1.202(2); angles (deg): C^5–O^1–C^1 111.75(14) and C^{12}–N^1–C^1 121.23(15).

1-deoxy-2,3-*O*-isopropylidene-1-(diphenylphosphinoyl)-1-(phenylamino)-D-glycerol (**IV**) crystallized spontaneously from the reaction mixture and could be isolated in a high yield (67%) (Scheme 1).

Scheme 1.



I **II** **IV**

This result is quite expectable, because the parent azomethine derived from triose is incapable of mutarotation and consists of 100% linear (syn and anti) forms of the free Shiff base. It readily undergoes the classical addition of the phosphorus compound at the C=N double bond (the Pudovik variant of the Kabachnik–Fields reaction [8, 9]).

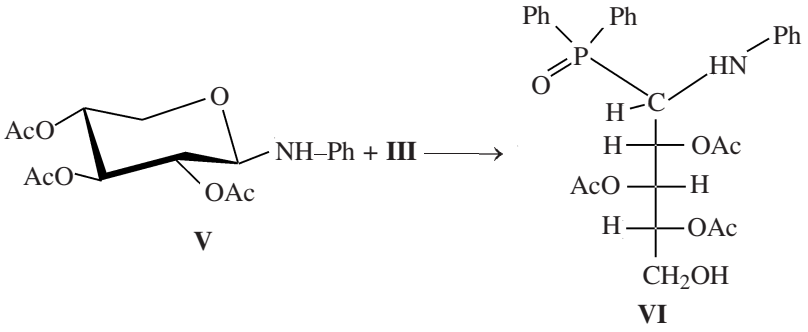
The pentose derivative involved in the reaction was 2,3,4-tri-*O*-acetyl-1-deoxy-1-(phenylamino)-D-xylopyranose (**V**) prepared alongside the procedure in [10, 11]. In our present work we determined its structure by X-ray diffraction analysis (Fig. 1), which was necessary for structural assessment of the most stable prevailing isomer in the reaction mixture. Under the reaction conditions, compound **V** can undergo mutarotation.

As follows from the X-ray diffraction data, molecule **V** in crystal is a β anomer. The pyranose ring has a $^4C_1$ conformation, and the C^1 and C^4 atoms deviate from the $C^2O^1C^3C^5$ ring plane by 0.73 and 0.69 Å, respectively. The phenyl group is planar, the sum of all bond angles in it is 358.4°. The dihedral angle between the NHPh fragment and the ring plane is 129.8°. The intermolecular hydrogen bonds N^1–$H^{1N}O^6$ [$x + 1$, y, z] in the crystal join molecules into chains running along the crystallographic axis *a*.

We established that the reaction of pyranosylaniline **V** with acid **III** proceeds by Scheme 2.

The reaction is complete in 18–20 h at 20°C. Adding pyridine to the reaction mixture almost halves the reaction time, which can be explained in terms of both accelerated mutarotation of the carbohydrate component mutarotation and accelerated isomerization of dipenylphosphinous acid into a reactve P(III) form.

Scheme 2.

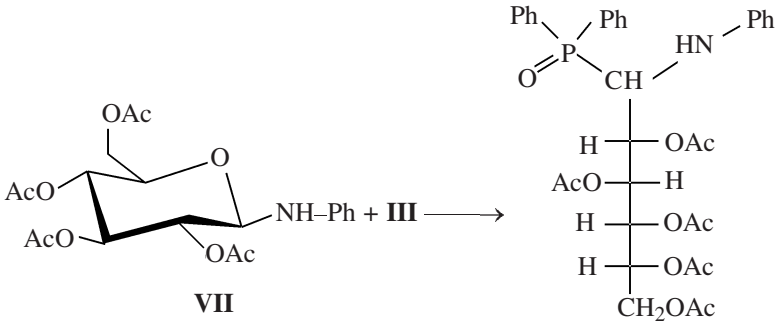


V **VI**

The yield of 2,3,4-tri-*O*-acetyl-1-deoxy-1-(diphenylphosphinoyl)-1-(phenylamino)-D-xylitol (**VI**) after chromatographic purification was 48.5%. Thus, the necessity of preliminary mutarotation of glycosylamine (conversion to the imino form) stipulates a longer reaction time as compared with the synthesis of α-amino-*tert*-phosphine oxide **IV**, all other reaction conditions being the same.

Another structurally similar substrate but derived from hexose, viz. 2,3,4,6-tetra-*O*-acetyl-1-deoxy-1-(phenylamino)-D-glucopyranose (**VII**) [10, 11], does not react with dipenylphosphinous acid at all without heating and adding a catalyst. This reaction could only be accomplished in the presence of pyridine or cadmium iodide under heating at 55–60°C for 10–12 h. The yield of α-amino-*tert*-phosphine oxide **VIII** was 30% or lower (Scheme 3).

Scheme 3.



VII **VIII**

Such a difference in the reactivity of aniline derivatives of pentose and hexose seems surprising. Note that the similarity of the steric structures of β-anomeric aniline derivatives of hexopyranose and xylopyranose is obvious from a comparison with data in [12]. The difference in the structures of β-glucopyranosylanilines derived from D-xylose and D-glucose consists in that the C^5 atom of the pyranose ring in the latter bears an acetoxymethyl substituent. This substituent can pose steric hindrance only in a cyclic glucosylamine, since in the imino form it resides at the periphery of the reacting molecule. Probably, the lower reactivity of compound **VII** is associated with restricted ring–chain isomerization as compared with the xylopyranose analog or with a different reaction mechanism: The process may involve substitution of the C–O fragment in the cyclic form of glycosylamine **VII** by a phosphinoyl group.

The next step of the study is investigation of the reaction of dipenylphosphinous acid with glycosylamines derived from D-mannose ketal, 1-deoxy-2,3;5,6-di-*O*-isopropylidene-1-(phenylamino)-β-D-mannofuranose (**IX**) and 2,3;5,6-di-*O*-cyclohexylidene-1-deoxy-1-(phenylamino)-β-D-mannofuranose (**X**). A preliminary communication concerning this part of investigation has been published in [2]. In the present work we studied the crystal structure of compound **IX** by X-ray diffraction (see table).

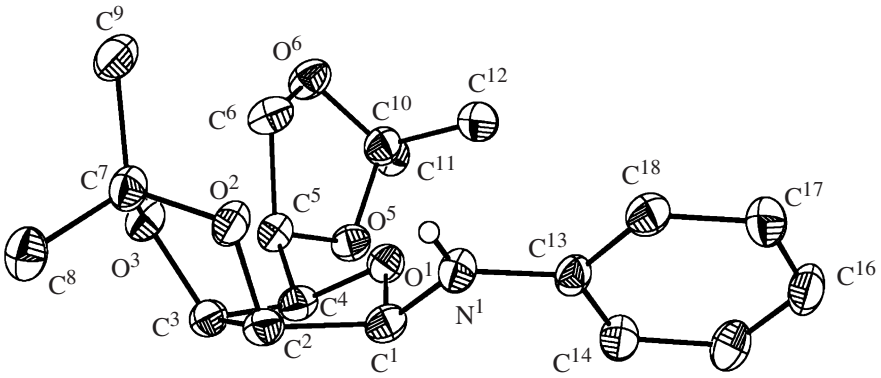


Fig. 2. General view of molecule **IX** with thermal ellipsoids drawn at the 50% probability level. Bond lengths (Å): O^2–C^2 1.424(4), O^2–C^7 1.437(4), O^1–C^4 1.436(4), O^1–C^1 1.461(4), O^3–C^7 1.430(5), O^3–C^3 1.438(4), N^1–C^{13} 1.400(4), N^1–C^1 1.412(5), O^6–C^{10} 1.425(5), O^6–C^6 1.428(5), O^5–C^5 1.435(4), and O^5–C^{10} 1.458(4); bond angles (deg): C^2–O^2–C^7 106.4(3), C^4–O^1–C^1 104.9(2), C^7–O^3–C^3 107.1(3), C^{13}–N^1–C^1 121.4(3), C^{10}–O^6–C^6 106.5(3), and C^5–O^5–C^{10} 109.7(3).

According to the X-ray diffraction data, compound **IX** is a β anomer containing the mannose residue in the furanose form ^{O1}ð with the O^1 atom deviating from the mean $C^1C^2C^3C^4$ plane by 0.56 Å and two dioxolane rings in the *envelope* conformation with the O^6 and C^7 atoms deviating from the corresponding ring planes by 0.49 and 0.50 Å, respectively (Fig. 2). The dihedral angle between the furanose and dioxolane ring planes is 116.3°. The phenyl ring is planar. Like in the crystal of **V**, molecules **IX** form N^1–$H^{1N}O^5$ [*x*, *y* + 1, *z*] hydrogen bonds which join the molecules into chains running along the crystallographic axis *a*.

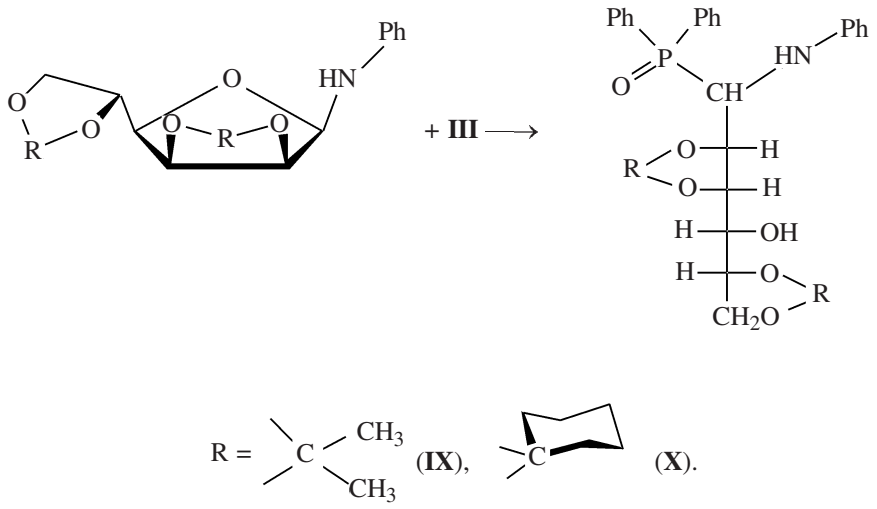
Furanozides **IX** and **X** react with compound **III** in even more rigid conditions (~60°C, 23–27 h) with pyridine as catalyst (Scheme 4).

The presence in ketals **IX** and **X** of additional cyclic structures undoubtedly decelerates mutarotation and probably retards sterically the attack of the P(III) reagent. The different size of the protective groups in **IX** and **X** affects to a certain degree the phosphorylation rate: The reaction time of the cyclohexylidene derivative is longer by 5 h as compared with the isopropylidene derivative. Products **XI** and **XII** were isolated by column chromatography on silica gel. The

Details of X-ray diffraction experiment and crystal data for compounds **V** and **IX**

Parameters	**V**	**IX**	Parameters	**V**	**IX**
Brutto formula	$C_{17}H_{21}NO_7$	$C_{18}H_{25}NO_5$	Scanning	ω	ω
Molecular weight	351.35	335.39	θ, deg	1.97–28.99	1.57–27.00
Difraktometr	Bruker SMART APEX II CCD	Bruker SMART 1000 CCD	Percentag of possible reflections measured (%)	99.8	99.2
Temperature, K	100(2)	120(2)			
Crystal system	Rhombic	Monoclynic	Number of measured reflections	10091	5725
Space group, *Z*	$P2_12_12_1$	$P2_1$			
a, Å	7.7687(9)	23.089(19)			
b, Å	13.0713(16)	6.751(6)	Number of unique reflections	2596 [0.0332]	2114 [R_{int} 0.0485]
c, Å	16.900(3)	12.326(10)			
β, deg		112.572(16)	Number of refined parameters	233	221
V, Å	1716.2(4)	1774(3)			
Z(*Z*′)	4(1)	2(1)	$R(F_{hkl})$: R_1	0.0340	0.0516
F(000)	744	720	wR_2	0.0878	0.1149
d_{calc}, g cm^{-1}	1.360	1.256	*GOF*	1.076	1.003
Linear absorption, μ, cm^{-1}	1.06	0.91	$\Delta\rho_{max}$, $\Delta\rho_{min}$, e Å^{-3}	0.28, –0.22	0.347, –0.233

Scheme 4.



R = C(CH3)2 (**IX**), C6H10 (**X**).

yields after purifications were 41 and 52%, respectively.

The synthesized compounds were all characterized by TLC, ^{1}H, ^{13}C and ^{31}P NMR spectroscopy and elemental analysis (see Experimental).

Products **VI**, **VIII**, **XI**, and **XII** are light yellow thick syrups, and compound **IV** is a powder with a high melting point. On TLC plates the products give slightly oblong spots with R_f 0.55–0.7. The ^{31}P NMR signals of the synthesized phosphine oxides appear at δ_P 28–31 ppm; therewith, compounds **IV**, **VI**, **XI**, and **XII** give by two signals, while compound **VIII**, only one signal. Hence, the addition of the hydrophosphoryl compound proceeds mainly nonstereospecifically to form a mixture of two optical isomers. The integral intensity ratios of the ^{1}H NMR signals of the protective groups and aromatic and carbohydrate fragments of compounds **IV**, **VI**, **VIII**, **XI** and **XII** confirm their structures. All proton signals display expected multiplicities and spin–spin coupling constants, e.g. the $^{2}J_{HP}$ for protons on C^1 is about 12 Hz. In the ^{13}C NMR spectra, the signals of carbon atoms proximate to phosphorus are split due to C–P spin–spin coupling. For example, the C^1 signals of **X** and **XI** are doublets in the characteristic region δ_C 50–52 ppm (J_{CP} 77.8 and 77.6 Hz, respectively). The C^2 signal of the carbohydrate fragments in **X** and **XI**, too, are split due to C–P spin–spin coupling ($^{2}J_{CP}$ 8.6 and 9.6 Hz, respectively).

Thus, glycosylamines derived from acetylated and ketalated trioses, pentoses, and hexoses are much less active in the Kabachnik–Fields reaction as compared with glycosamines derived from free monosaccharides, and protected monoses undergo no furanization on phosphorylation. The reaction with dipenylphosphinous acid probably occur nonstereospecifically and afford mixtures of optical isomers. To conclude, we thus proposed an unique synthetic approach to α-aminophosphoryl compounds derived from glycosylamines and synthesized a series of new α-amino-*tert*-phosphine oxides that contain a carbohydrate fragment in their structures and hold promise in terms of diverse physiological activity.

EXPERIMENTAL

All experiments with P(III) reagents were carried out under dry argon with solvents purified and dried according to conventional procedures [13].

The ^{31}P NMR spectra were measured on a Bruker WP-80 spectrometer at 32.4 MHz against external reference 85% H_3PO_4. The ^{1}H NMR spectra were measured a Bruker H-250 spectrometer at 250 MHz against residual proton signals of the deuterated solvent. The ^{13}C NMR spectra were measured on a Bruker AMX-400 at 100.61 MHz against residual proton signals of the deuterated solvent.

Thin-layer chromatography was carried out on Silufol UV-254 plates, development by calcination. Adsorption chromatography was carried out on a silica gel L 40–100 μm column, eluents benzene–acetonitrile–hexane, 4 : 2 : 1 (A) and benzene–dioxane, 3 : 1 (B).

The X-ray diffraction study was carried out on a Bruker Smart diffractometer at 100 K (MoK_α radiation, $2\theta_{max}$ 52.00°). The structure was solved by the direct method, all non-hydrogen atoms were located in difference Fourier synthesis maps and refined anisotropically on F^2_{hkl}. Hydrogen atoms were located in difference Fourier synthesis maps and refined iso-

tropically in the rigid body approximation. All calculations were performed using the SHELXTL 5.10 program suite [14].

1-Deoxy-2,3-*O*-isopropylidene-1-(diphenylphosphinoyl)-1-(phenylamino)-D-glycerol (IV). Aniline, 0.93 g, was added with stirring at room temperature under argon to a solution of 1.3 g of 2,3-*O*-isopropylidene-D-glycerose in benzene. After 30 min, 2.02 g of dipenylphosphinous acid was added to the mixture, and stirring was continued for 2.5 h. The precipitate that formed was filtered off, washed with ether, and dried in a vacuum. Yield 2.45 g (67%). Light yellow powder, mp 208–210°C. ^{31}P NMR spectrum (acetone-d_6), δ_P, ppm: 28.95 (50%), 29.2 (50%). ^{1}H NMR spectrum (acetone-d_6) δ, ppm: glycerol fragment, 2.03–2.08 m (6H, CH_3); 3.6–3.8 m (2H, C^3H), 4.10 m (1H, C^2H), 6. 35 m (1H, C^1H, $^2J_{HP}$ 16.05 Hz); aniline fragment, 6.30 br.s (1H, NH), 6.66 d (2H, C^2H, C^6H, $^3J_{HH^3}$ 7.56 Hz); 7.05 t (1H, C^4H, $^3J_{HH^3}$ 8.4 Hz); 7.41 d.d (2H, C^3H, C^5H, $^3J_{HH^4}$ 8.4 Hz, 3JHH2,6 7.56 Hz); diphenylphosphinoyl fragment, 7.47 m (3H, C^3H, C^4H, C^5H); 7.58 m (3H, $C^{3'}H$, $C^{4'}H$, $C^{5'}H$) 7.83 m (2H, C^2H, C^6H, $^3J_{HP}$ 10.96 Hz), 7.89 m (2H, C^2H, C^6H, $^3J_{HP}$ 10.96 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: glycerol fragment, 26.2–27.1 m (H_3C–C–CH_3); 55.6 d (C^1, $^1J_{CP}$ 74.8 Hz); 63.8 d (C^3, $^3J_{CP}$ 5.2 Hz); 98.6 d (C^2, $^2J_{CP}$ 8.7 Hz); 121.3 [O^2–$C(CH_3)_2$–O^3]; aniline fragment, 113.8 (C^2, C^6); 118.6 (C^4); 128.6 (C^3, C^5); 132.4 d (C^1, $^3J_{CP}$ 3.8 Hz); diphenylphosphinoyl fragment, 128.6–129.2 m ($2C^3$, $2C^5$); 130.8–131.9 m ($2C^1$, $2C^4$, $2C^2$, $2C^6$). Found, %: C 70.84, 70.82; H 6.28, 6.32; N 2.98, 3.03; P 7.55, 7.58. $C_{24}H_{26}NO_3P$. Calculated, %: C 70.76; H 6.39; N 3.44; P 7.62.

2,3,4-Tri-*O*-acetyl-1-deoxy-1-(diphenylphosphinoyl)-1-(phenylamino)-D-xylitol (VI). Dioxane, 3 ml, was added with stirring under argon to a mixture of 0.2 g of dipenylphosphinous acid and 0.32 g of 2,3,4-tri-*O*-acetyl-1-deoxy-1-(phenylamino)-D-xylopyranose, and the mixture was left to stand for a day at room temperature. After complete reaction, the solution was concentrated and passed through a column of silica gel (eluent B); the fraction with R_f 0.65–0.75 was collected. Yield 0.25 g (48.5%). Colorless syrup. ^{31}P NMR spectrum (acetone-d_6), δ_P, ppm: 27.6 (32%), 28.2 (68%). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: carbohydrate fragment, 1.92–2.01 m (9H, CH_3); 3.74 m [H, C^5H, $^2J_{H,H^{5'}}$ 10.41 Hz, $^3J_{H,H^4}$ 5.49 Hz, $^3J_{H,H(OH)}$ 2.56 Hz]; 3.84 m [1H, $C^{5'}H$, $^3J_{H,H^5}$ 10.41 Hz, $^3J_{H,H^4}$ 5.49 Hz, $^3J_{H,H(OH)}$ 2.59 Hz]; 4.77 m (1H, C^2H, $^3J_{H,H^1}$ 8.53 Hz); 4.93 m (1H, C^4H, $^3J_{H,H^5}$ 5.49 Hz); 5.32 m (1H, C^3H); 5.54 m [1H, C^1H, $^3J_{H,H^2}$ 8.53 Hz, $^2J_{HP}$ 12.05 Hz, $^3J_{H,H(NH)}$ 7.67 Hz]; 6.36 m (1H, OH, $^3J_{H,H^{5'}}$ 2.59 Hz, $^3J_{H,H^5}$ 2.56 Hz); aniline fragment, 5.92 m (1H, NH, $^3J_{H,H^1}$ 7.67 Hz), 6.88 d (2H, C^2H, C^6H, $^3J_{HH^3}$ 7.69 Hz); 7.05 t (1H, C^4H, $^3J_{HH^3}$ 6.67 Hz); 7.26 d.d (2H, C^3H, C^5H, $^3J_{HH^4}$ 6.67 Hz, $^3J_{HH^{2,6}}$ 7.67 Hz); diphenylphosphinoyl fragment, 7.47 m (3H, C^3H, C^4H, C^5H); 7.63 m (3H, $C^{3'}H$, $C^{4'}H$, $C^{5'}H$) 7.84 m (2H, C^2H, C^6H, $^3J_{HP}$ 11.10 Hz), 8.11 m (2H, C^2H, C^6H, $^3J_{HP}$ 11.10 Hz). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: carbohydrate fragment, 19.7–21.6 m [H_3C–C(O)]; 51.1 d (C^1, $^1J_{CP}$ 80.49 Hz); 57.8 (C^5); 62.1 (C^4); 67.4 d (C^2, $^2J_{CP}$ 24.15 Hz); 69.4 d (C^3, $^3J_{CP}$ 13.08 Hz); 142.8 [O^4–C(O)–CH_3]; 161.5 [O^3–C(O)–CH_3]; 169.7 [O^2–C(O)–CH_3]; aniline fragment, 110.5 (C^2, C^6); 114.4 (C^4); 128.6 (C^3, C^5); 146.2 d (C^1, $^3J_{CP}$ 5.5 Hz); diphenylphosphinoyl fragment, 128.3–128.7 m ($2C^3$, $2C^5$); 130.6–131.2 d ($2C^1$, $^1J_{CP}$ 10.1 Hz); 131.5–132.3 m ($2C^4$, $2C^2$, $2C^6$). Found, %: C 62.79, 62.84; H 5.84, 5.85; N 2.54, 2.55; P 5.52, 5.53. $C_{29}H_{32}NO_8P$. Calculated, %: C 62.93; H 5.79; N 2.62; P 5.61.

2,3,4,6-Tetra-*O*-acetyl-1-deoxy-1-(diphenylphosphinoyl)-1-(phenylamino)-D-glucitol (VIII). Dipenylphosphinous acid, 0.4 g, and 2.5 ml of pyridine (or 0.1 g of CdI_2) were added under argon to a solution of 0.42 g of 2,3,4,6-tetra-*O*-acetyl-1-deoxy-1-(phenylamino)-D-glucopyranose in 5 ml of chloroform. The reaction mixture was heated at 55–60°C, stirred for 12 h, diluted with 15 ml of ethanol, decolorized by refluxing with 1 g of charcoal, filtered, concentrated in a vacuum, and passed through a column of silica gel (eluent B). The fraction with R_f 0.55–0.6 was collected. Yield 0.2 g (29.8%). Syrup. ^{31}P NMR spectrum (acetone-d_6), δ_P, ppm: 30.6. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: carbohydrate fragment, 1.96–1.99 m (12H, CH_3); 4.04 m (H, C^6H); 4.09 m (1H, $C^{6'}H$); 4.20 m (1H, C^5H); 4.80 m (1H, C^4H); 4.93 m (1H, C^3H); 5.23 m [1H, C^1H, $^3J_{H,H^2}$ 5.12 Hz, $^2J_{HP}$ 12.08 Hz, $^3J_{H,H(NH)}$ 5.48 Hz]; 5.54 m (1H, C^2H, $^3J_{H,H^1}$ 5.12 Hz); 6.87 m (1H, OH); aniline fragment, 6.46 m (H, NH, $^3J_{H,H^1}$ 5.48 Hz), 7.27 d (2H, C^2H, C^6H, $^3J_{HH^3}$ 8.41 Hz); 7.33 t (H, C^4H, $^3J_{HH^3}$ 7.27 Hz); 7.38 d.d (2H, C^3H, C^5H, $^3J_{HH^4}$ 7.27 Hz, $^3J_{HH^{2,6}}$ 8.41 Hz); diphenylphosphinoyl fragment, 7.50 m (3H, C^3H, C^4H, C^5H); 7.60 m (3H, $C^{3'}H$, $C^{4'}H$, $C^{5'}H$) 7.85 m (2H, C^2H, C^6H, $^3J_{HP}$ 11.09 Hz), 8.12 m (2H, C^2H, C^6H, $^3J_{HP}$ 11.09 Hz). ^{13}C NMR spectrum (acetone-d_6), δ_P, ppm: carbohydrate fragment, 13.6

[H_3C–C(O)–O^6]; 19.7 [H_3C–C(O)–O^2, H_3C–C(O)–O^3]; 23.7 [H_3C–C(O)–O^4]; 61.8 d (C^1, $^1J_{CP}$ 80.49 Hz); 66.7 (C^6); 67.5 (C^5); 68.7 d (C^3, $^3J_{CP}$ 5.8 Hz); 71.4 d (C^2, $^2J_{CP}$ 8.5 Hz); 72.8 (C^4); 169.3 [O^6–C(O)–CH_3]; 169.6 [O^3–C(O)–CH_3]; 169.8 [O^2–C(O)–CH_3]; 170.0 [O^4–C(O)–CH_3]; aniline fragment, 114.2 (C^2, C^6); 119.1 (C^4); 128.6 (C^3, C^5); 132.5 d (C^1, $^3J_{CP}$ 2.1 Hz); diphenylphosphinoyl fragment, 128.5–129.0 m ($2C^3$, $2C^5$); 131.0–131.5 m ($2C^1$, $2C^4$, $2C^2$, $2C^6$). Found, %: C 61.05, 61.10; H 5.79, 5.78; N 2.54, 2.52; P 4.59, 4.54. $C_{34}H_{38}NO_{11}P$. Calculated, %: C 61.17; H 5.70; N 2.62; P 4.65.

***tert*-Phosphine oxides XI–XII** *(general procedure).* A solution of 1-deoxy-2,3;5,6-di-*O*-isopropylidene-(cyclohexylidene)-1-(phenylamino)-β-D-mannofuranose, 0.05 mol, and 0.05 mol of dipenylphosphinous acid in a mixture of 5 ml of chloroform and 3 ml of pyridine was stirred under argon for 23–27 h at 60°C. The solvent was then removed in a vacuum, and the residue was purified by chromatography on silica gel in system A. Products **XI** are **XII** were isolated as yellow syrups crystallized with time, soluble in most organic solvents, and isoluble in water.

1-Deoxy-1-2,3;5,6-di-*O*-isopropylidene-1-(diphenylphosphinoyl)-1-(phenylamino)-D-mannitol (XI). Yield 41%. R_f 0.66. ^{31}P NMR spectrum (DMSO-d_6), δ_P, ppm: 29.5 (31.3%); 31.0 (68.7%). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: carbohydrate fragment, 25.3–27.3 m (H_3C–C–CH_3); 54.7 d (C^1, $^1J_{CP}$ 77.8 Hz); 66.4 (C^6); 69.6 (C^4); 74.9 d (C^3, $^3J_{CP}$ 5.4 Hz); 76.0 (C^5); 80.2 d (C^2, $^2J_{CP}$ 8.6 Hz); 108.2 [O^2–$C(CH_3)_2$–O^3]; 108.8 [O^5–$C(CH_3)_2$–O^6]; aniline fragment, 112.8 (C^2, C^6); 116.5 (C^4); 128.6 (C^3, C^5); 147.3 d (C^1, $^3J_{CP}$ 3.5 Hz); diphenylphosphinoyl fragment, 127.6–128.2 m ($2C^3$, $2C^5$); 130.6–133.7 m ($2C^1$, $2C^4$, $2C^2$, $2C^6$). Found, %: C 67.28, 67.29; H 6.57, 6.60; N 2.54, 2.55; P 5.89, 5.92. $C_{30}H_{36}NPO_6$. Calculated, %: C 67.16; H 6.53; N 2.62; P 5.78.

2,3;5,6-Di-*O*-cyclohexylidene-1-deoxy-1-(diphenylphosphinoyl)-1-(phenylamino)-D-mannitol (XII). Yield 52%. R_f 0.85. ^{31}P NMR spectrum (DMSO-d_6), δ_P, ppm: 28.4 (40.65%); 30.9 (59.35%). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: carbohydrate fragment, 21.2–24.4, 34.2–36.1 m (H^2C, cyclohexylidene); 54.2 d (C^1, $^1J_{CP}$ 77.6 Hz); 65.7 (C^6); 69.0 (C^4); 73.4 d (C^3, $^3J_{CP}$ 3.4 Hz); 78.9 (C^5); 79.8 d (C^2, $^2J_{CP}$ 9.6 Hz); 108.3 [O^2–$C(CH_2)_5$–O^3]; 108.6 [O^5–$C(CH_2)_5$–O^6]; aniline fragment, 112.2 (C^2, C^6); 116.0 (C^4); 128.2 (C^3, C^5); 146.7 d (C^1, $^3J_{CP}$ 3.1 Hz); diphenylphosphinoyl fragment, 127.5–128.7 m ($2C^3$, $2C^5$); 130.4–133.5 m ($2C^1$, $2C^4$, $2C^2$, $2C^6$). Found, %: C 70.15, 70.19; H 7.25, 7.22; N 2.13, 2.12; P 5.36, 5.29. $C_{36}H_{44}NPO_6$. Calculated, %: C 70.02; H 7.13; N 2.27; P 5.02.

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