The use of cesium dibenzyl and diphenyl phosphates for stereoselective synthesis of glycosyl phosphate derivatives

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Peracetates of β-glycosyl dibenzyl phosphates are formed efficiently in the reaction of cesium dibenzyl phosphate with peracetyl-α-glycosyl nitrates derived from L-fucopyranose, D-galactopyranose, and 2-azido-2-deoxy-D-galactopyranose or with tri-*O*-acetyl-α-L-fucopyranosyl bromide. On the contrary, the reaction of the above-mentioned glycosyl nitrates with cesium diphenyl phosphate leads to thermodynamically more stable α-glycosyl diphenyl phosphate *via* intermediate formation of the corresponding β-anomers.

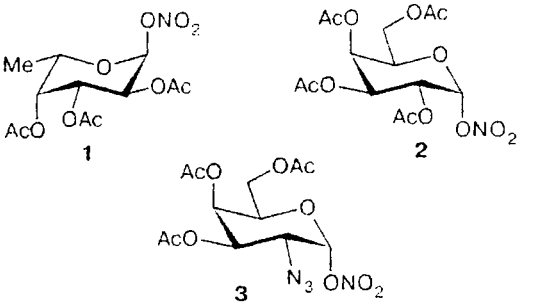
Key words: glycosyl nitrates, glycosyl phosphates, phosphorylation, stereospecificity.

In recent years,[1,2] enzymatic and chemo-enzymatic syntheses of oligosaccharides and glycoconjugates involving the use of glycosyl transferases have been intensively developing. In this connection, the preparation of the precursors of their biosynthesis, namely, nucleoside and polyprenyl glycosyl diphosphates, becomes quite important.

Glycosyl phosphates are key compounds in the chemical and enzymatic synthesis of these derivatives.[3,4] Various approaches to the chemical synthesis of glycosyl phosphates are documented. In the approach based on nucleophilic substitution at the C(1) atom in carbohydrate derivatives, dibenzyl and diphenyl phosphates or their salts are often used as the reagents. Acylated glycosyl halides serve as typical substrates in this reaction, although the use of *O*-glycosyl trichloroacetimidates, thioglycosides, pent-4-enyl glycosides, and bicyclic derivatives of sugars for this purpose has also been described (see a review[4]).

Recently, we demonstrated that the reaction of 2-azido-3,4-di-*O*-acetyl-2,6-dideoxy-α-L-galactopyranosyl nitrate with cesium dibenzyl phosphate in DMF smoothly gives the corresponding β-glycosyl dibenzyl phosphate.[5] The discovery of the previously unknown transformation of glycosyl nitrates into glycosyl phosphates on treatment with cesium dibenzyl phosphate[6] stimulated us to perform a more detailed investigation on the possible application of this reaction in the synthesis of glycosyl phosphate derivatives.

As the starting compounds, peracetylated α-glycosyl nitrates derived from 6-deoxy-L-galactopyranose (L-fucopyranose (**1**)), D-galactopyranose (**2**), and 2-azido-2-deoxy-D-galactopyranose (**3**)) were chosen. The use of these compounds makes it possible to study the influence of the nature of the substituent at C(2) and the presence of the deoxy unit at C(6) on the rate of the reaction and the stereochemistry of the resulting products for monosaccharide derivatives with the *galacto*-configuration.



The possibility of using glycosyl nitrates in the nucleophilic addition at C(1) had been demonstrated earlier by converting them into glycosyl acetates,[7–9] glycosyl halides,[8] glycosyl xanthates,[9] and methyl,[7,10] allyl,[10] and benzyl glycosides[11,12] by reactions with the corresponding alkoxides. The transformation of peracetyl-β-D-glycosyl nitrates into 1,2-orthoesters[13] has been described and several methods for the conversion of glycosyl nitrates into derivatives with a free OH group at C(1) have been developed.[14–16]

Glycosyl nitrates derived from 2-azido-2-deoxyhexoses are easily prepared by azidonitration of the corresponding glycals; we used this method[8] to prepare nitrate **3**. Nitrate **2** was synthesized[7] by the reaction of penta-*O*-acetyl-β-D-galactopyranose with $HNO_3/CHCl_3$. The ^1H NMR spectral data for the reaction product correspond to those reported in the literature.[13] Nitrate **1** was unknown previously as well as similar derivatives of other 6-deoxyhexoses. We showed that this compound can be smoothly synthesized (the yield of the crystalline product is 65%) by treatment of tetra-*O*-acetyl-L-fucopyranose with 100% HNO_3 in dichloromethane. The starting compound is a mixture of α- and β-anomers (85 : 15) and, thus, in this case, unlike the reaction with hexose derivatives, the acetate group at C(1) in the α-anomer peracetate is also easily replaced. The structure of compound **1** is confirmed by the IR spectrum,

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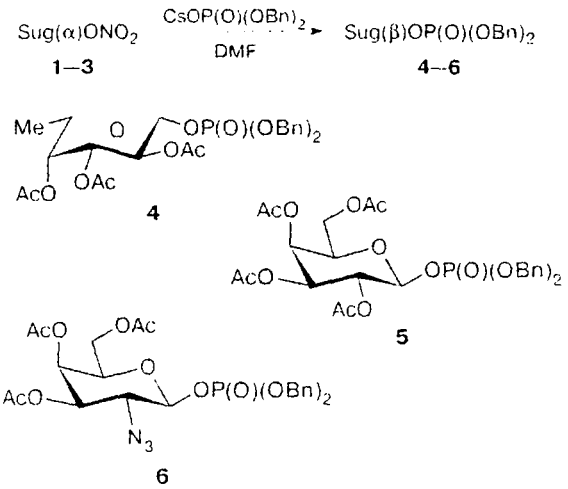
which contains an absorption band typical of the ONO_2 group (ν_{max} 1650 cm^{-1}); the data of the ^1H NMR (δ 6.43, d, $J_{1,2}$ = 3.4 Hz, H(1)) and ^{13}C NMR (δ 96.4) spectra indicate the α-configuration of the C(1) atom.

The possibility of using nitrate **1** for the synthesis of β-L-fucopyranosyl phosphate is of the greatest interest. The synthesis of this important glycosyl phosphate has been the subject of several studies.[17–21] In these studies, the instability of phosphotriester **4** and its easy isomerization to the thermodynamically more stable α-isomer were noted.



Hereinafter, Sug is a sugar residue.

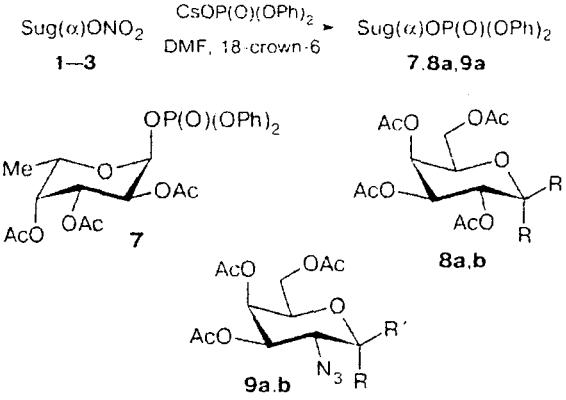
As in the reaction with 2-azido-3,4-di-*O*-acetyl-2,6-dideoxy-α-L-galactopyranosyl nitrate,[5,6] the reaction of nitrate **1** with $CsOP(O)(OBn)_2$ in DMF proceeds smoothly at 20 °C. Phosphotriester **4**, isolated after 3 h in 64% yield, contains, apparently, no α-anomer impurity, as indicated by the ^1H and ^{13}C NMR spectra, which correspond to those reported in the literature.[17a,18,21] Thus, $CsOP(O)(OBn)_2$ is suitable for the synthesis of β-glycosyl dibenzyl phosphates also when an acetoxy group is attached to the C(2) atom of the sugar residue instead of the azido group.

Efficient formation of β-glycosyl dibenzyl phosphates was also demonstrated in the reaction of $CsOP(O)(OBn)_2$ with glycosyl nitrates **2** and **3**, derived from D-galactose and 2-azido-2-deoxy-D-galactose. As may be expected, the replacement of the Me group at C(5) of monosaccharide by the CH_2OAc group decreases the rate of nucleophilic substitution at C(1). After 12 h at 20 °C, the yields of phosphotriesters **5** and **6** were 75% and 89%, respectively. The data of ^1H and ^{13}C NMR spectra confirm the structures of the compounds. In the case of compound **5**, the spectra coincide with those described previously.[22] In the case of **6**, the chemical shifts and multiplicities of the signals most significant for establishing the configuration are those for H(2) (δ 3.83, dd, $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 10.7 Hz), C(1) (δ 97.5, d, $J_{1,P}$ = 4.8 Hz) and C(2) (δ 60.8, d, $J_{2,P}$ = 6.8 Hz).

The ready availability and the purity of the starting compounds, mild reaction conditions, the formation of the stereochemically uniform product with the inverted configuration at the anomeric center, and the high product yields make the reaction of acylated glycosyl nitrates with cesium dibenzyl phosphate an attractive method for the synthesis of glycosyl phosphates.

We also investigated the possibility of using this reagent for the synthesis of glycosyl phosphates from glycosyl bromides. The reaction of 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide with $CsOP(O)(OBn)_2$ in DMF for 1 h smoothly furnishes compound **4** in 82% yield. The NMR spectra of phosphotriester **4** prepared by this reaction are identical to the spectra of phosphotriester **4** synthesized by the reaction with nitrate **1**.

As noted above, in the synthesis of glycosyl phosphates based on the nucleophilic substitution at the C(1) atom of monosaccharide, apart from dibenzyl phosphate, diphenyl phosphate is widely used as the reagent; in this case, the reaction normally yields thermodynamically more stable α-anomers of the glycosyl phosphate derivatives.[4] Thus *O*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl) trichloroacetimidate reacts with $(BnO)_2P(O)OH$ to afford β-phosphate **4**, while its reaction with $(PhO)_2P(O)OH$ affords α-phosphate derivative (**7**).[18] The transformations of tetra-*O*-acetyl-α-D-galactopyranosyl bromide into β-glycosyl phosphate through the reaction with $AgOP(O)(OBn)_2$[23] and into the corresponding α-anomer upon reaction with $AgOP(O)(OPh)_2$[24] are also known. We were interested whether a similar regularity is obeyed with cesium salts and studied the reaction of $CsOP(O)(OPh)_2$ with glycosyl nitrates **1**–**3** under conditions comparable to those used in the reaction with $CsOP(O)(OBn)_2$. The solubility of cesium diphenyl phosphate in DMF is much lower than the solubility of cesium dibenzyl phosphate; we managed to obtain a homogeneous solution by adding 18-crown-6 to the reaction mixture.



8a,9a: R = $OP(O)(OPh)_2$, R′ = H;
8b,9b: R = H, R′ = $OP(O)(OPh)_2$

Under these conditions, fucose derivative **1** smoothly reacts with $CsOP(O)(OPh)_2$ at 20 °C; after 12 h,

α-phosphate **7** can be isolated in 60% yield. The ^{1}H and ^{13}C NMR spectra of the product correspond to those described previously.[18,25] Thus, the use of cesium diphenyl phosphate allows the synthesis of thermodynamically more stable α-anomer of glycosyl phosphate. In the reactions with glycosyl nitrates **2** and **3**, the reaction also yields α-anomers **8a** and **9a** as the final reaction products. However, in these cases, it is possible to demonstrate the intermediate formation of β-phosphates **8b** and **9b**, which are gradually converted into the corresponding α-anomers. Thus the product isolated after the reaction of galactosyl nitrate **2** with $CsOP(O)(OPh)_2$ performed for 12 h at 20 °C is a 1 : 6 mixture of phosphates **8a** and **8b**, according to the data of ^{1}H NMR spectra (*cf.* Ref. 25). Pure α-phosphate **8a** can be obtained (in 60% yield) when the reaction is carried out for 12 h at 55 °C.

When the reaction was performed with 2-azido-2-deoxygalactose derivative **3** for 2 h at 50 °C, the isolated product was found to be a 1 : 1 mixture of α- and β-phosphates **9a** and **9b**. After additional heating (12 h, 37 °C), the ratio of the components in the mixture became equal to 4 : 1. In this case, the most characteristic ^{1}H NMR signals used to determine the anomer ratio in the mixture are the signals of H(1) (δ 6.05, dd, $J_{1,2}$ = 3.4 Hz, $J_{1,P}$ = 6.4 Hz) and H(3) (δ 5.31, dd, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.2 Hz), which correspond to the α-isomer and the signals with δ 5.22 (t, $J_{1,2}$ = $J_{1,P}$ = 7.6 Hz, H(1)) and 4.86 (dd, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.2 Hz, H(3)), which correspond to the β-isomer.

These results demonstrate that, as in the case with $CsOP(O)(OBn)_2$, the primary reaction product is formed upon the substitution at the C(1) atom with inversion of configuration; in the case of the diphenyl phosphate derivative, it undergoes the second inversion of configuration at the anomeric center. Thus, the reaction of glycosyl nitrates with cesium diphenyl phosphate can be used to prepare α-glycosyl phosphate derivatives.

Experimental

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 K on a Bruker WM-250 spectrometer using acetone as the internal standard. ^{31}P NMR spectra were recorded in $CDCl_3$ at 300 K on a Bruker AM-200 spectrometer using external 85% H_3PO_4 as the standard. The optical rotation was measured on a Jasco DIP-360 automated polarimeter. IR spectra were measured on a Perkin-Elmer spectrophotometer. Thin layer chromatography was performed in glass plates with a fixed silica gel layer (Merck). Column chromatography was carried out with silica gel LiChroprep Si 60 (Merck). Chemicals were purchased from Sigma, except for 18-crown-6 (Fluka). The solvents DMF, CH_2Cl_2, and MeCN were distilled from CaH_2 *in vacuo* and stored over 4 Å molecular sieves. The cesium salts of phosphodiesters were prepared by mixing dibenzyl hydrogen phosphate or diphenyl hydrogen phosphate with 1.01 equiv. of Cs_2CO_3 in MeCN. The solvent was distilled off and the residue was dried *in vacuo* at 25 °C.

Tri-*O*-acetyl-α-L-fucopyranosyl nitrate (1). A mixture of 100% HNO_3 (d = 1.52) (6 mL) and CH_2Cl_2 (9 mL) was added dropwise at 0 °C to a solution of tetra-*O*-acetyl-L-fucopyranose[21] (593 mg, 1.78 mmol) (a 85 : 15 mixture of α- and β-isomers, ^{1}H NMR data) in 3 mL of anhydrous CH_2Cl_2. The reaction mixture was stirred for an additional 5 h and poured in ice water, the organic phase was separated, washed three times with ice water, a saturated solution of $NaHCO_3$, and again with water, and dried with Na_2SO_4, and the solvent was evaporated *in vacuo*. The resulting crystalline material was recrystallized from an Et_2O–petroleum ether mixture to give 388 mg (65%) of compound **1**, m.p. 79–80 °C, $[\alpha]^{29}_D$ −142.3° (*c* 1.5, $CHCl_3$), R_f 0.34 (petroleum ether–EtOAc, 2 : 1). Found (%): C, 43.35; H, 5.37; N, 4.38. $C_{12}H_{17}NO_{10}$. Calculated (%): C, 42.99; H, 5.11; N, 4.18. IR (KBr), ν/cm^{-1}: 1750 (OAc); 1650 (ONO_2); 1370; 1250 (ONO_2); 1080; 830. ^{1}H NMR, δ: 1.18 (d, 3 H, H(6), $J_{5,6}$ = 6.9 Hz); 2.06 (s, 3 H, OAc); 2.13 (s, 3 H, OAc); 2.21 (s, 3 H, OAc); 4.32 (br.q, 1 H, H(5)); 5.23–5.46 (m, 3 H, H(2), H(3), H(4)); 6.43 (d, 1 H, H(1), $J_{1,2}$ = 3.4 Hz). ^{13}C NMR, δ: 15.8 (C(6)); 20.6 (CO<u>Me</u>); 65.6 (C(2)); 67.4 (C(4)); 67.9 (C(3)); 70.2 (C(5)); 96.4 (C(1)); 169.8, 170.1, 170.3 (all <u>C</u>OMe).

Dibenzyl 2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl phosphate (4). $CsOP(O)(OBn)_2$ (92 mg, 0.25 mmol) was added at 20 °C to a solution of compound **1** (50 mg, 0.15 mmol) in 0.13 mL of anhydrous DMF and the mixture was stirred for 3 h. The reaction mixture was diluted with 5 mL of $CHCl_3$ and poured into brine. The organic layer was separated, washed with water, and dried with Na_2SO_4, and the solvent was evaporated *in vacuo*. Column chromatography in the toluene–EtOAc (3 : 1) + 2% Et_3N system gave 53 mg (64%) of phosphate **4**, R_f 0.32 (petroleum ether–EtOAc, 1 : 1). ^{1}H NMR, δ: 1.22 (d, 3 H, H(6), $J_{5,6}$ = 6.9 Hz); 1.92 (s, 3 H, OAc); 1.98 (s, 3 H, OAc); 2.19 (s, 3 H, OAc); 3.92 (br.q, 1 H, H(5)); 5.01–5.12 (m, 5 H, H(1), C<u>H</u>$_2$Ph); 5.24–5.32 (m, 3 H, H(2), H(3), H(4)); 7.29–7.36 (m, 10 H, <u>Ph</u>). ^{13}C NMR, δ: 15.9 (C(6)); 20.5(CO<u>Me</u>); 68.7 (C(2), J = 9.8 Hz); 69.5; 69.6; 69.7; 70.2; 70.8; 96.7 (C(1), J = 4.3 Hz); 127.8, 128.0, 128.5, 128.6 (all CPh); 169.8, 170.0, 170.5 (all <u>C</u>OMe) (*cf.* Ref. 19).

Dibenzyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl phosphate (5) was prepared similarly to phosphate **4** from nitrate **2**[7] (75 mg, 0.191 mmol) and $CsOP(O)(OBn)_2$ (109 mg, 0.29 mmol) in 0.15 mL of anhydrous DMF; the reaction time was 12 h. Column chromatography in the toluene–EtOAc (2 : 1) + 2% Et_3N system gave 87 mg of phosphate **5** (yield 75%), R_f 0.30 (petroleum ether–EtOAc, 1 : 1). ^{1}H NMR (C_6D_6), δ: 1.48 (s, 3 H, OAc); 1.49 (s, 3 H, OAc); 1.64 (s, 3 H, OAc); 1.66 (s, 3 H, OAc); 3.27 (m, 1 H, H(5)); 3.98 (d, 2 H, C<u>H</u>$_2$Ph, $J_{H,P}$ = 7.0 Hz); 4.92 (d, 2 H, C<u>H</u>$_2$Ph, $J_{H,P}$ = 7.0 Hz); 4.95–5.03 (m, 2 H, H(6,6')); 5.11 (dd, 1 H, H(3), $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.4 Hz); 5.37 (dd, 1 H, H(4), $J_{4,5}$ = 1.0 Hz); 5.47 (t, 1 H, H(1), $J_{1,2}$ = $J_{1,P}$ = 7.8 Hz); 5.74 (dd, 1 H, H(2)); 6.96–7.16 (m, 10 H, Ph). ^{13}C NMR, δ: 20.5 (CO<u>Me</u>); 61.1 (C(6)); 66.7 (C(4)); 68.7 (d, C(2), J = 8.7 Hz); 69.7, 69.9 (both CH_2Ph); 70.5 (C(3)); 71.8 (C(5)); 96.8 (d, C(1), J = 4.7 Hz); 127.8, 127.9, 128.2, 128.6 (all CPh); 169.5, 169.9, 170.0, 170.2 (all C<u>C</u>OMe) (*cf.* Ref. 22).

2-Azido-2-deoxy-3,4,6-tri-*O*-acetyl-β-D-galactopyranosyl dibenzyl phosphate (6) was prepared similarly to phosphate **4** from nitrate **3**[8] (30 mg, 0.08 mmol) and $CsOP(O)(OBn)_2$ (49 mg, 0.12 mmol) in 0.1 mL of anhydrous DMF; the reaction time was 12 h. Column chromatography in the toluene–EtOAc (3 : 1) + 2% Et_3N system gave 42 mg of phosphate **6** (yield 89%), $[\alpha]^{29}_D$ −3.86° (*c* 1.5, $CHCl_3$). ^{1}H NMR, δ: 1.95 (s, 3 H, OAc); 2.07 (s, 3 H, OAc); 2.18 (s, 3 H, OAc); 3.83 (dd, 1 H, H(2), $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 10.4 Hz); 4.01 (m, 1 H, H(5)); 4.08–4.20 (m, 2 H, H(6,6')); 4.88 (dd, 1 H, H(3), $J_{3,4}$ = 3.5 Hz); 5.10–5.20 (m, 5 H, H(1), C<u>H</u>$_2$Ph); 5.38 (dd, 1 H, H(4), $J_{4,5}$ = 1.0 Hz); 7.36 (m, 10 H, Ph). ^{13}C NMR, δ: 20.5(CO<u>Me</u>); 60.8 (d, C(2), J = 8.6 Hz); 61.0 (C(6)); 66.0 (C(4)); 69.5, 69.6, 69.8; 71.1 (C(3)); 71.7 (C(5)); 97.5 (d, C(1),

J = 4.8 Hz); 127.8, 128.2, 128.6, 129.0, 135.3 (all Ph); 169.5, 169.9, 170.2 (all COMe). ^{31}P NMR: δ −2.12.

Dibenzyl 2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl phosphate (4) from 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide. A solution of $CsOP(O)(OBn)_2$ (250 mg, 0.35 mmol) in 0.3 mL of anhydrous DMF was added at 0 °C to a solution of bromide **10** [21] (80 mg, 0.230 mmol) in 0.30 mL of anhydrous DMF. The mixture was stirred for 10 min at 0 °C and for 50 min at 20 °C. The reaction mixture was diluted with 5 mL of $CHCl_3$ and poured into brine. The organic layer was separated, washed with water, and dried with Na_2SO_4, and the solvent was evaporated *in vacuo*. Column chromatography in the toluene—EtOAc (3 : 1) + 2% Et_3N system gave 97 mg (82%) of phosphate **4**; according to TLC and ^{1}H NMR data, it was identical to the sample prepared from nitrate **1**.

2,3,4-Tri-*O*-acetyl-α-L-fucopyranosyl diphenyl phosphate (7). $CsOP(O)(OPh)_2$ (125 mg, 0.328 mmol) and 18-crown-6 (85 mg, 0.328 mmol) were added at 20 °C to a solution of nitrate **1** (55 mg, 0.164 mmol) in 0.15 mL of anhydrous DMF. The reaction mixture was stirred for 12 h, diluted with 5 mL of $CHCl_3$, and poured into brine. The organic layer was separated, washed with water, and dried with Na_2SO_4, and the solvent was evaporated *in vacuo*. Column chromatography in the toluene—EtOAc (3 : 1) + 2% Et_3N system gave 51 mg (60%) of phosphate **7**, R_f 0.37 (petroleum ether—EtOAc, 1 : 1). ^{1}H NMR, δ: 1.03 (d, 3 H, H(6), $J_{5,6}$ = 6.9 Hz); 1.86 (s, 3 H, OAc); 2.01 (s, 3 H, OAc); 2.16 (s, 3 H, OAc); 4.21 (q, 1 H, H(5), $J_{5,6}$ = 6.9 Hz); 5.22 (ddd, 1 H, H(2), $J_{1,2}$ = 3.4 Hz, $J_{2,P}$ = 2.8 Hz, $J_{2,3}$ = 10.6 Hz); 5.30 (d, 1 H, H(4), $J_{3,4}$ = 2.8 Hz); 5.36 (dd, 1 H, H(3)); 6.08 (dd, 1 H, H(1), $J_{1,P}$ = 6.3 Hz); 7.21—7.38 (m, 10 H, Ph) (*cf.* Ref. 18).

2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl diphenyl phosphate (8) was prepared similarly to phosphate **7** from nitrate **2** (75 mg, 0.191 mmol) and $CsOP(O)(OPh)_2$ (136 mg, 0.382 mmol) in the presence of 18-crown-6 (90 mg, 0.382 mmol) in 0.15 mL of anhydrous DMF; the reaction time was 12 h at 55 °C. Column chromatography in the toluene—EtOAc (2 : 1) + 2% Et_3N system gave 66 mg of phosphate **5** (yield 60%). R_f 0.41 (petroleum ether—EtOAc, 1 : 1). ^{1}H NMR, δ: 1.83 (s, 3 H, OAc); 1.92 (s, 3 H, OAc); 2.01 (s, 3 H, OAc); 2.14 (s, 3 H, OAc); 3.92 (m, 1 H, H(6′)); 4.11 (m, 1 H, H(6)); 4.38 (m, 1 H, H(5)); 5.23 (ddd, 1 H, H(2), $J_{1,2}$ = 3.2 Hz, $J_{2,P}$ = 2.8 Hz, $J_{2,3}$ = 10.4 Hz); 5.39 (dd, 1 H, H(3), $J_{3,4}$ = 3.1 Hz); 5.51 (dd, 1 H, H(4), $J_{4,5}$ = 1.0 Hz); 6.13 (dd, 1 H, H(1), $J_{1,P}$ = 6.4 Hz); 7.12—7.42 (m, 10 H, Ph). ^{13}C NMR, δ: 20.5, 20.6 (both COMe); 61.1 (C(6)); 66.9 (d, C(2), J = 6.9 Hz); 67.5 (C(4)); 68.9 (C(3)); 77.2 (C(5)); 95.8 (d, C(1), J = 4.8 Hz); 120.2, 120.3, 120.4, 125.8, 128.3, 129.1, 129.9 (all Ph); 170.0 (COMe) (*cf.* Ref. 25).

2-Azido-2-deoxy-3,4,6-tri-*O*-acetyl-D-galactopyranosyl diphenyl phosphate (a mixture of α- and β-isomers) (9a,b) was prepared similarly to phosphate **7** from nitrate **3** (90 mg, 0.240 mmol) and $CsOP(O)(OPh)_2$ (183 mg, 0.480 mmol) in the presence of 18-crown-6 (126 mg, 0.480 mmol) in 0.35 mL of anhydrous DMF; the reaction time was 12 h at 55 °C. Column chromatography in the toluene—EtOAc (3 : 1) + 2% Et_3N system gave 89 mg (63%) of phosphate **9** as a mixture of α- and β-isomers in 4 : 1 ratio. ^{1}H NMR, δ: 1.86 (s, 2.4 H, α-OAc); 1.97 (s, 0.6 H, β-OAc); 2.04 (s, 0.6 H, β-OAc); 2.07 (s, 2.4 H, α-OAc); 2.14 (s, 0.6 H, β-OAc); 2.17 (s, 2.4 H, α-OAc); 3.80—3.91 (m, α-H(6′), 2β-H); 3.94—4.13 (m, 2.2 H, α-H(2), α-H(6), β-H(5), β-H(6,6′)); 4.30 (m, 0.8 H, α-H(5)); 4.86 (dd, 0.2 H, β-H(3), $J_{2,3}$ = 10.8 Hz, $J_{3,4}$ = 3.4 Hz); 5.23 (t, 0.2 H, β-H(1), $J_{1,2}$ = $J_{1,P}$ = 7.6 Hz), 5.30 (dd, 0.8 H, α-H(3), $J_{2,3}$ = 10.8 Hz, $J_{3,4}$ = 3.2 Hz); 5.36 (d, 0.2 H, β-H(4)); 5.46 (d, 0.8 H, α-H(4)); 6.02 (dd, 0.8 H, α-H(1), $J_{1,2}$ = 3.6 Hz, $J_{1,P}$ = 6.2 Hz), 7.16—7.41 (m, 10 H, Ph). ^{31}P NMR, δ: −15.1 (α-isomer); −15.5 (β-isomer).

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