ISSN 1070-4280, Russian Journal of Organic Chemistry, 2019, Vol. 55, No. 4, pp. 508–513. © Pleiades Publishing, Ltd., 2019.
Russian Text © The Author(s), 2019, published in Zhurnal Organicheskoi Khimii, 2019, Vol. 55, No. 4, pp. 608–614.

Phosphorylated Glycoconjugates Based on Isosteviol, D-Arabinofuranose, and D-Ribofuranose

R. R. Sharipova[a], M. G. Belenok[a], I. Yu. Strobykina[a], and V. E. Kataev[a]*

[a] *Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center, Russian Academy of Sciences, ul. Akademika Arbuzova 8, Kazan, 420029 Tatarstan, Russia*
**e-mail: kataev@iopc.ru*

Received April 5, 2018; revised February 10, 2019; accepted February 19, 2019

Abstract—First phosphorylated glycoconjugates were synthesized in three stages on the basis of isosteviol, D-arabinofuranose, and D-ribofuranose. In the first stage, isosteviol reacted with methyl 5-*O*-(*p*-tosyl)-2,3-di-*O*-benzoyl-D-ribofuranoside and methyl 5-*O*-(*p*-tosyl)-2,3-di-*O*-benzoyl-D-arabinofuranoside to give glycoconjugates in which the diterpenoid fragment is linked through ester bond to the carbohydrate C^5 atom. In the second stage, the anomeric methoxy group in the furanoside fragment was replaced by bromine, and the resulting 2,3-di-*O*-benzoyl-D-ribofuranosyl and 2,3-di-*O*-benzoyl-D-arabinofuranosyl bromides were treated with dibutyl phosphate to afford the target phosphorylated derivatives.

Keywords: isosteviol, arabinofuranose, ribose, glycoterpenoids, glycoconjugates, glycosides.

DOI: 10.1134/S1070428019040158

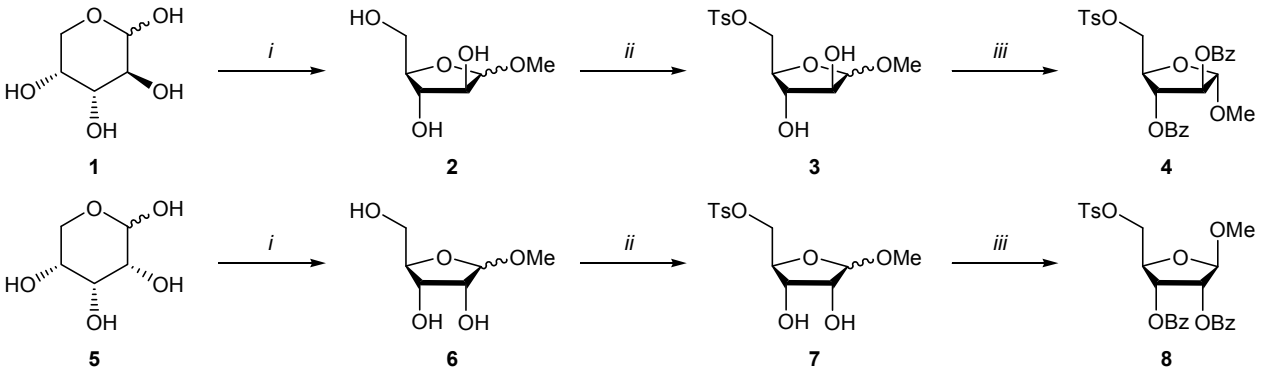
Secondary metabolites isolated from various natural sources are widely used as starting compounds for the design of new therapeutic agents. An example is diterpenoid isosteviol **9** (16-oxo-*ent*-beyeran-19-oic acid) which is obtained by acid hydrolysis of glycosides from *Stevia rebaudiana* [1]; glycoside extract from that plant is sold as a low-calorie sweetener under different trade names in distribution networks. Like all natural terpenoids, isosteviol is a biologically active compound exhibiting moderate antihyperglycemic [2, 3], cardioprotective [4], anticancer [2, 5], antitubercular [6], anti-inflammatory [2], antibacterial, and antifungal activities [7]. Chemical modification of isosteviol not only enhanced its antitubercular [6, 8–10], anticancer [12, 13], and antibacterial activities [14] but also endowed it with antiviral and [15] and antimitotic properties [16].

In continuation of our works on the synthesis and biological activity of isosteviol [17], betulin [18, 19], and allobetulin glycoconjugates [20] with various monosaccharides, herein we describe the first synthesis of phosphorylated isosteviol glycoconjugates with D-arabinofuranose and D-ribofuranose.

In the first stage, D-arabinopiranose **1** was converted to methyl 5-*O*-*p*-tosyl-α/β-D-arabinofuranoside **3** according to the procedure described in [21], and benzoylation of **3** gave methyl 5-*O*-*p*-tosyl-2,3-di-*O*-benzoyl-α-D-arabinofuranoside **4** (Scheme 1). Likewise, from D-ribose **5** we obtained methyl 5-*O*-*p*-tosyl-2,3-di-*O*-benzoyl-β-D-ribofuranoside **8**.

In the second stage, glycosides **4** and **8** were conjugated to isosteviol **9** via reaction in acetonitrile in the presence of potassium carbonate under argon. Glycoconjugates **10** and **12** thus formed were isolated in 43 and 21% yield, respectively, by silica gel column chromatography (Scheme 2). The formation of **10** and **12** was confirmed by their MALDI mass spectra which showed ion peaks with *m*/*z* 695.29 $[M + Na]^+$ ($C_{40}H_{48}NaO_9$, *M* 695.32) (**10**) and *m*/*z* 695.42 $[M + Na]^+$ ($C_{40}H_{48}NaO_9$, *M* 695.32), 711.41 $[M + K]^+$ ($C_{40}H_{48}KO_9$, *M* 711.29) (**12**). Glycoconjugate **10** was isolated as a single α-anomer. This followed from the ^1H and ^{13}C NMR spectra which contained only one set of signals; the anomeric proton resonated in the ^1H NMR spectrum as a singlet at δ 5.11 ppm (cf. [22]). Compound **12** was pure β-anomer, and its anomeric proton resonated as a singlet at δ 5.14 ppm (cf. [23]). The methoxy group in **10** was replaced by bromine by the action of acetyl bromide [24]. Bromide **11** was obtained in quantitative yield (Scheme 2) and was treated with dibutyl phosphate **14** in the presence of ethyl(diisopropyl)amine according to the procedure

Scheme 1.

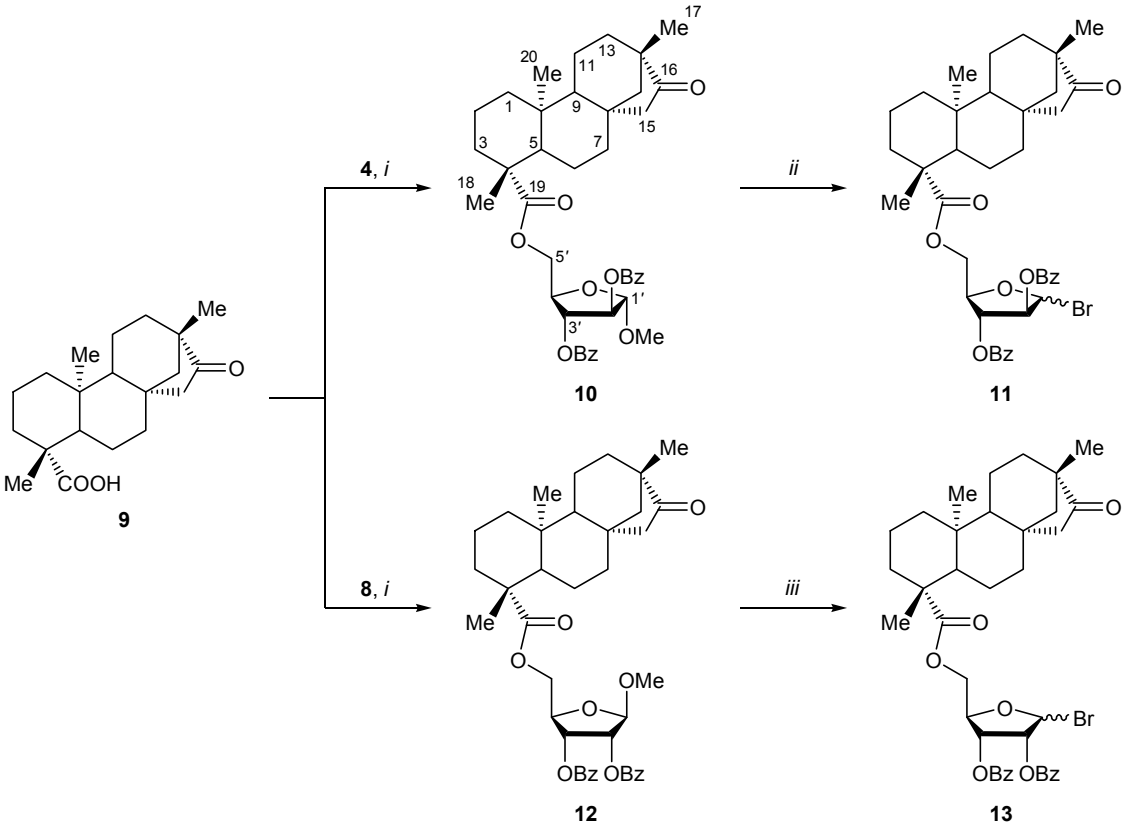


i: HCl, MeOH, 0–20°C, 24 h; *ii*: TsCl, Py, 0–20°C, 24 h; *iii*: BzCl, Py, 0–20°C, 24 h; *iv*: H_2SO_4, MeOH, 0–20°C, 24 h.

described in [25]; the molar ratio **11**–(*i*-Pr)$_2$NEt-–**14** was 1:4:4, and the concentration of **11** was 0.003 M (cf. [25]). Phosphorylated glycoconjugate **15** was isolated in 29% yield by chromatography (Scheme 3). The MALDI mass spectrum of **15** displayed a ion peak with *m*/*z* 873.53 $[M + Na]^+$ ($C_{47}H_{63}NaO_{12}P$, *M* 873.40). In the ^{1}H NMR spectrum of **15** we observed a doublet signal at δ 6.01 ppm with a vicinal coupling constant of 5.0 Hz due to anomeric proton of the α-anomer [22] and a multiplet at 5.75–5.79 ppm due to anomeric proton of the β-isomer [23]. The signal intensity ratio was 3.3 in favor of the α-anomer. This is consistent with the data of [25], according to which the stereoselectivity in the glycosylation of dibutyl phosphate **14** depends on the concentration of 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl bromide.

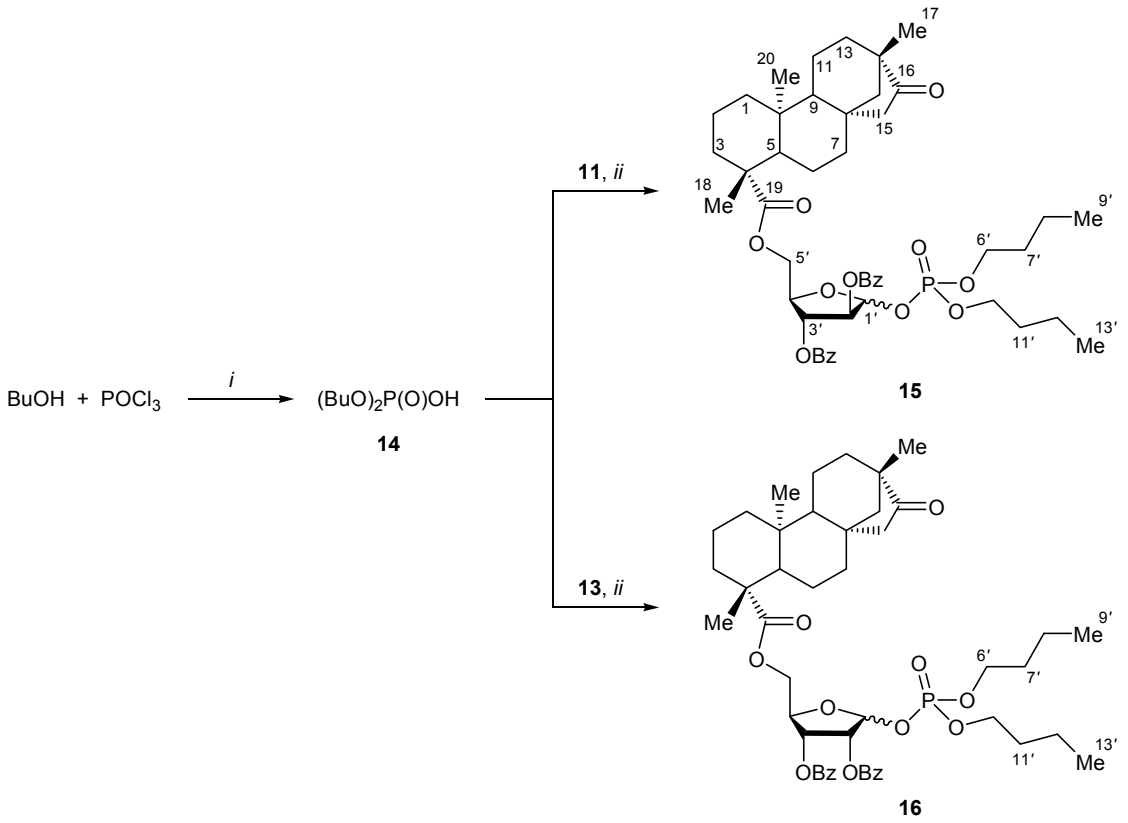
The methoxy group in **12** was quantitatively replaced by bromine using 33% HBr in AcOH [26].

Scheme 2.



i: K_2CO_3, MeCN, 80°C, 60 h; *ii*: AcBr, CH_2Cl_2, 0°C, 3 h; *iii*: HBr–AcOH, 0°C, 4 h.

Scheme 3.



i: Et_3N, toluene, 60°C, 1 h; *ii*: $(i\text{-Pr})_2NEt$, MeCN, 20°C, 12 h.

Bromide **13** without further purification was treated with dibutyl phosphate **14** (the reactant ratio was the same as in the phosphorylation of **11**) to obtain 32% (isolated yield) of phosphorylated glycoconjugate **16** (Scheme 3). The MALDI mass spectrum of **16** contained a ion peak with *m*/*z* 873.40 $[M + Na]^+$ ($C_{47}H_{63}NaO_{12}P$, *M* 873.40). The ^1H NMR spectrum of **16** showed a doublet at δ 6.03 ppm (^3J = 5.7 Hz) and a multiplet at δ 5.73–5.75 ppm due to anomeric protons of the β- and α-anomers, respectively [23], with an intensity ratio of 2:1 in favor of the β-anomer.

As far as we know, compounds **15** and **16** are the first phosphorylated glycoconjugates of terpenoids with monosaccharides. Study of biological activity of the synthesized compounds is now in progress.

EXPERIMENTAL

The ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker Avance-400 spectrometer (Germany) at 400 (^1H) and 100.6 MHz (^{13}C, ^{31}P); the ^1H and ^{13}C chemical shifts were measured relative to the residual proton and carbon signals of the solvent ($CDCl_3$). The MALDI mass spectra were recorded on a Bruker Daltonik UltraFlex III TOF/TOF instrument operating in the linear mode (Nd:YAG laser, λ 355 nm; positive ion detection, a.m.u. range 200–6000; samples were applied to a metal target from solutions in methanol with a concentration of 10^{-3} mg/mL; *p*-nitroaniline was used as matrix); the data were processed by FlexAnalysis 3.0 (Bruker Daltonik, Germany). The optical rotations were measured at λ 589 nm (20°C) on a Perkin Elmer-341 polarimeter (USA). The progress of reactions and the purity of the isolated compounds were monitored by thin-layer chromatography on Sorbfil plates (*Imid* Ltd., Krasnodar, Russia); spots were visualized by treatment with a 5% solution of sulfuric acid, followed by heating to 120°C.

D-Arabinose and D-ribose were commercial products (Acros, Belgium). Methyl α/β-D-arabinofuranoside **2**, methyl 5-*O*-*p*-tosyil-α/β-D-arabinofuranoside **3**, methyl α/β-D-ribofuranoside **6**, methyl 5-*O*-*p*-tosyl-α/β-D-ribofuranoside **7**, methyl 5-*O*-*p*-tosyl-2,3-di-*O*-benzoyl-α-D-arabinofuranoside **4**, and methyl 5-*O*-*p*-tosyl-2,3-di-*O*-benzoyl-β-D-ribofuranoside **8** were synthesized as described in [21, 27]. The spectral

parameters of glycosides **4** and **8** were consistent with published data [22, 23]. Isosteviol **9** [28] was isolated from Sweta natural sweetener (Stevian Biotechnology) according to the procedure reported in [1]. Dibutyl phosphate **14** was prepared as described in [29].

Glycoconjugates 10 and 12 (*general procedure*). A solution of 1.08 mmol of methyl 5-*O*-*p*-tosyl-2,3-di-*O*-benzoyl-α-D-arabinofuranoside **4** or methyl 5-*O*-*p*-tosyl-2,3-di-*O*-benzoyl-β-D-ribofuranoside **8** in 10 mL of acetonitrile was added dropwise with stirring under argon to a mixture of 1 mmol of isosteviol **9** in 40 mL of acetonitrile and 4 mmol of potassium carbonate. The mixture was refluxed for 20–30 h, the precipitate was filtered off, the filtrate was concentrated under reduced pressure, and the residue was diluted with water and extracted with chloroform. The extract was dried over $MgSO_4$, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate at a ratio of 6:1 to isolate conjugate **10** or at a ratio of 10:1 to isolate conjugate **12**. The products were isolated as white amorphous powders.

Methyl 5-*O*-(16,19-dioxo-*ent*-beyeran-19-yl)-2,3-di-*O*-benzoyl-α-D-arabinofuranoside (10). Yield 0.33 g (43%), $[\alpha]_D^{20}$ = –53.0° (*c* = 1, CH_2Cl_2). ^{1}H NMR spectrum, δ, ppm: 0.75 s (3H, $C^{20}H_3$), 0.96 s (3H, $C^{17}H_3$), 1.23 s (3H, $C^{18}H_3$), 0.81–1.95 m (18H), 2.21 d (1H, 3-H_{eq}, *J* = 12.9 Hz), 2.62 d.d (1H, 15-H_{ax}, *J* = 18.7, 3.7 Hz), 3.47 s (3H, OCH_3), 4.32–4.48 m (3H, 4′-H, 5′-H), 5.11 s (1H, 1′-H), 5.44–5.50 m (2H, 2′-H, 3′-H), 7.42–8.08 m (10H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.19 (C^{20}), 18.74 (C^2), 19.68 (C^{17}), 20.16 (C^{11}), 21.51 (C^6), 28.74 (C^{18}), 37.15 (C^3), 37.71 (C^{10}), 37.87 (C^{12}), 39.26 (C^{13}), 39.63 (C^1), 41.32 (C^7), 43.80 (C^4), 48.23 (C^8), 48.51 (C^{15}), 54.15 (C^{14}), 54.59 (C^9), 54.81 (C^5), 57.03 (OCH_3), 63.10 ($C^{5'}$), 77.55 ($C^{4'}$), 79.55 ($C^{3'}$), 82.47 ($C^{2'}$), 106.69 ($C^{1'}$), 128.32 (C_{arom}), 129.75 d (C_{arom}), 133.35 d (C_{arom}), 165.33 (Ph**C**=O), 165.47 (Ph**C**=O), 176.73 (C^{19}), 222.13 (C^{16}). Mass spectrum: *m*/*z* 695.29 $[M + Na]^+$. Found, %: C 71.63; H 7.17. $C_{40}H_{48}O_9$. Calculated, %: C 71.41; H 7.19. *M* 672.80.

Methyl 5-*O*-(16,19-dioxo-*ent*-beyeran-19-yl)-2,3-di-*O*-benzoyl-β-D-ribofuranoside (12). Yield 0.16 g (21%), $[\alpha]_D^{20}$ = –48.0° (*c* = 0.9, CH_2Cl_2). ^{1}H NMR spectrum, δ, ppm: 0.75 s (3H, $C^{20}H_3$), 0.97 s (3H, $C^{17}H_3$), 1.22 s (3H, $C^{18}H_3$), 0.81–1.96 m (18H), 2.21 d (1H, 3-H_{eq}, *J* = 13.5 Hz), 2.64 d.d (1H, 15-H_{ax}, *J* = 18.7, 3.7 Hz), 3.46 s (3H, OCH_3), 4.23–4.42 m (2H, 5′-H), 4.58–4.62 m (1H, 4′-H), 5.14 s (1H, 1′-H), 5.59–5.62 m (1H, 2′-H), 5.64–5.69 m (1H, 3′-H), 7.28–8.01 m (10H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.82 (C^{20}), 19.43 (C^2), 20.31 (C^{17}), 20.79 (C^{11}), 22.14 (C^6), 29.44 (C^{18}), 37.80 (C^3), 38.29 (C^{10}), 38.50 (C^{12}), 39.91 (C^{13}), 40.24 (C^1), 41.93 (C^7), 44.41 (C^4), 48.93 (C^8), 49.15 (C^{15}), 54.78 (C^{14}), 55.21 (C^9), 55.98 (C^5), 57.67 (OCH_3), 65.61 ($C^{5'}$), 73.24 ($C^{4'}$), 75.83 ($C^{3'}$), 79.53 ($C^{2'}$),107.07 ($C^{1'}$), 128.76–133.88 (C_{arom}), 165.72 (Ph**C**=O), 165.83 (Ph**C**=O), 177.39 (C^{19}), 222.89 (C^{16}). Mass spectrum, *m*/*z*: 695.42 $[M + Na]^+$, 711.41 $[M + K]^+$. Found, %: C 71.35; H 7.22. $C_{40}H_{48}O_9$. Calculated, %: C 71.41; H 7.19. *M* 672.80.

5-*O*-(16,19-Dioxo-*ent*-beyeran-19-yl)-2,3-di-*O*-benzoyl-D-arabinofuranosyl bromide (11). A solution of 0.3 g (0.48 mmol) of conjugate **10** in 10 mL of anhydrous methylene chloride was cooled to 0°C, 0.2 mL (2.6 mmol) of acetyl bromide was added, and 0.08 mL (2.1 mmol) of anhydrous methanol in 1 mL of anhydrous methylene chloride was added dropwise. The mixture was stirred for 3 h at 0°C, diluted with 20 mL of methylene chloride, and washed with ice water (2×20 mL) and with a saturated solution of sodium hydrogen carbonate (2×50 mL). The organic phase was filtered through a layer of $MgSO_4$, and the solvent was removed under reduced pressure. Bromide **11** was isolated in quantitative yield as a white amorphous powder and was immediately used in the next stage.

5-*O*-(16,19-Dioxo-*ent*-beyeran-19-yl)-2,3-di-*O*-benzoyl-D-ribofuranosyl bromide (13). A solution of 0.14 g (0.2 mmol) of conjugate **12** in 5 mL of anhydrous methylene chloride was cooled to 0°C, 0.3 mL of a 33% solution of HBr in acetic acid was added, and the mixture was stirred for 4 h, allowing it to gradually warm up 20°C. The mixture was poured into 10 mL of ice water, and the organic phase was separated, washed with water (2×10 mL), dried over Na_2SO_4, and evaporated under reduced pressure. Bromide **13** was isolated in quantitative yield as a white amorphous powder and was immediately used in the next stage.

Phosphates 15 and 16 (*general procedure*). Bromide **11** or **13**, 1 mmol, was dissolved in 50 mL of anhydrous acetonitrile, and 4 mmol of dibutyl phosphate **14** and 4 mmol of ethyl(diisopropyl)amine in 50 mL of anhydrous acetonitrile were added. The mixture was stirred for 12 h at 20°C under argon, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (6:1) as eluent to isolate phosphate **15** or **16** as a transparent oil.

Dibutyl 5-*O*-(16,19-dioxo-*ent*-beyeran-19-yl)-2,3-di-*O*-benzoyl-α/β-D-arabinofuranosyl phosphate

(15). Yield 0.1 g (29%), $[\alpha]_D^{20}$ = –10.6° (*c* = 0.5, CH_2Cl_2); α/β ratio 3.3. ^{1}H NMR spectrum, δ, ppm: 0.70 s (3H, $C^{20}H_3$, α), 0.72 s (1H, $C^{20}H_3$, β), 0.90 t (6H, *J* = 7 Hz, $C^{9'}H_3$, $C^{13'}H_3$, α), 0.92 t (2H, *J* = 6.9 Hz, $C^{9'}H_3$, $C^{13'}H_3$, β), 0.94 s (3H, $C^{17}H_3$, α), 0.95 s (1H, $C^{17}H_3$, β), 1.19 s (3H, $C^{18}H_3$, α), 1.21 s (1H, $C^{18}H_3$, β), 0.79–1.94 m [33.8H (α) and 0.3H (β), *ent*-beyerane skeleton, 7′-H, 8′-H, 11′-H, 12′-H], 2.16-2.22 m (1.6H, 3-H_{eq}), 2.56-2.64 m (1.6H, 15-H_{ax}), 3.94–4.16 m (5.5H, 6′-H, 10′-H), 4.28–4.46 m (2.9H, 5′-H), 4.61–4.73 m (1.6H, 4′-H), 5.47–5.49 m (1.6H, 3′-H), 5.59–5.61 m (1.6H, 2′-H), 5.75–5.79 m (0.3H, 1′-H, β), 6.01 d (1H, *J* = 5.0 Hz, 1′-H, α), 7.39–8.12 m (13H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.41 (C^{20}), 13.67 ($C^{9'}$, $C^{13'}$), 19.05 ($C^{8'}$, $C^{12'}$), 19.96 (C^2), 20.42 (C^{17}), 20.44 (C^{11}), 21.75 (C^6), 29.01 (C^{18}), 32.41 ($C^{7'}$), 32.45 ($C^{11'}$), 37.42 (C^3), 38.11 (C^{10}), 38.16 (C^{12}), 39.52 (C^{13}), 39.57 (C^1), 41.54 (C^7), 44.05 (C^4), 48.48 (C^8), 48.76 (C^{15}), 54.41 (C^{14}), 54.49 (C^9), 54.89 (C^5), 57.31 ($C^{5'}$, β), 63.19 ($C^{5'}$, α), 68.02 d.d ($C^{6'}$, $C^{10'}$, *J* = 12.7, 5.9 Hz), 77.24 ($C^{4'}$, β), 77.83 ($C^{4'}$, α), 82.16 ($C^{3'}$, β), 82.28 ($C^{3'}$, α), 82.66 ($C^{2'}$, β), 83.19 ($C^{2'}$, α), 101.07 ($C^{1'}$, β), 103.05 d ($C^{1'}$, *J* = 5.3 Hz, α), 128.63 (C_{arom}), 128.72 d (C_{arom}), 130.03 d (C_{arom}), 133.92 (C_{arom}), 165.12 (Ph**C**=O), 165.57 (Ph**C**=O), 176.84 (C^{19}), 222.24 (C^{16}). ^{31}P NMR spectrum, δ_P, ppm: –3.33 (α), –0.68 (β). Mass spectrum: *m*/*z*: 873.53 $[M + Na]^+$. Found, %: C 66.43; H 7.48; P 3.66. $C_{47}H_{63}O_{12}P$. Calculated, %: C 66.34; H 7.46; P 3.64. *M* 850.97.

Dibutyl 5-*O*-(16,19-dioxo-*ent*-beyeran-19-yl)-2,3-di-*O*-benzoyl-α/β-D-ribofuranosyl phosphate (16). Yield 0.11 g (32%), $[\alpha]_D^{20}$ = –20.0° (*c* = 0.8, CH_2Cl_2), α/β ratio 0.5. ^{1}H NMR spectrum, δ, ppm: 0.71 s (3H, $C^{20}H_3$, β), 0.73 s (1.5H, $C^{20}H_3$, α), 0.91–0.95 m (9H, $C^{9'}H_3$, $C^{13}H_3$), 0.96 s (3H, $C^{17}H_3$, β), 0.97 s (1.5H, $C^{17}H_3$, α), 1.20 s (4.5H, $C^{18}H_3$), 0.82–1.96 m [39H (β) and 0.5H (α), *ent*-beyerane skeleton, 7′-H, 8′-H, 11′-H, 12′-H], 2.19 d (1.5H, *J* = 13.1 Hz, 3-H_{eq}), 2.58–2.69 m (1.5H, 15-H_{ax}), 4.06–4.16 m (6H, 6′-H, 10′-H), 4.27–4.54 m (3H, 5′-H), 4.59–4.68 m (1.5H, 4′-H), 5.41–5.46 m (0.5H, 3′-H, α), 5.60 br.s (1H, 3′-H, β), 5.62–5.66 m (0.5H, 2′-H, α), 5.73–5.75 m [1.5H, 1′-H (α), 2′-H (β)], 6.03 d (1H, *J* = 5.7 Hz, 1′-H, β), 7.33–8.01 m (15H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.49 (C^{20}), 13.67 ($C^{11'}$, $C^{15'}$), 18.77, 19.08 ($C^{10'}$, $C^{14'}$), 19.98 (C^2), 20.00 (C^{17}), 20.45 (C^{11}), 21.79 (C^6), 29.03 (C^{18}), 32.34 ($C^{9'}$, $C^{13'}$), 37.44 (C^3), 38.12 (C^{10}), 38.17 (C^{12}), 39.53 (C^{13}), 39.58 (C^1), 41.51 (C^7), 44.06 (C^4), 48.52 (C^8), 48.78 (C^{15}), 54.42 (C^{14}), 54.86 (C^9, C^5), 57.28 ($C^{5'}$, β), 64.71 ($C^{5'}$, α), 67.50 d ($C^{8'}$, $C^{12'}$, *J* = 5.9 Hz), 72.07 ($C^{4'}$, α), 72.50 ($C^{4'}$, β), 75.80 d ($C^{3'}$, *J* = 9.1 Hz, α), 76.32 ($C^{3'}$, β), 79.57 d ($C^{2'}$, *J* = 17.1 Hz, β), 80.31 d ($C^{2'}$, *J* = 16.0 Hz, α), 100.50 ($C^{1'}$, α), 102.43 d ($C^{1'}$, *J* = 3.5 Hz, β), 128.53 (C_{arom}), 129.93 (C_{arom}), 133.74 (C_{arom}), 165.03 (Ph**C**=O), 165.44 (Ph**C**=O), 176.92 (C^{19}), 222.45 (C^{16}). ^{31}P NMR spectrum, δ_P, ppm: –2.81 (β), –0.58 (α). Mass spectrum, *m*/*z*: 873.68 $[M + Na]^+$, 889.72 $[M + K]^+$. Found, %: C 66.31; H 7.51; P 3.60. $C_{47}H_{63}O_{12}P$. Calculated, %: C 66.34; H 7.46; P 3.64. *M* 850.97.

ACKNOWLEDGMENTS

The authors thank the Assigned Spectral–Analytical Center (Kazan Scientific Center, Russian Academy of Sciences) for technical support.

CONFLICT OF INTERESTS

The authors declare the absence of conflict of interests.

REFERENCES

1. Khaibullin, R.N., Strobykina, I.Yu., Kataev, V.E., Lodochnikova, O.A., Gubaidullin, A.T., and Musin, R.Z., *Russ. J. Gen. Chem*., 2009, vol. 79, p. 967. doi 10.1134/S107036320905017X
2. Chatsudthipong, V. and Muanprasat, C., *Pharmacol. Ther*., 2009, vol. 121, p. 41. doi 10.1016/j.pharmthera.2008.09.007
3. Ma, J., Ma, Z., Wang, J., Milne, R.W., Xu, D., Davey, A.K., and Evans, A.M., *Diabetes, Obes. Metab*., 2007, vol. 9, p. 597. doi 10.1111/j.1463-1326.2006.00630.x
4. Xu, D., Li, L., Wang, J., Davey, A.K., Zhang, S., and Evans, A.M., *Life Sci*., 2007, vol. 80, p. 269. doi 10.1016/j.lfs.2006.09.008
5. Mizushina, Y., Akihisa, T., Ukiya, M., Hamasaki, Y., Murakami-Nakai, C., Kuriyama, I., Takeuchi, T., Sugawara, F., and Yoshida, H., *Life Sci*., 2005, vol. 77, p. 2127. doi 10.1016/j.lfs.2005.03.022
6. Kataev, V.E., Militsina, O.I., Strobykina, I.Yu., Kovylyaeva, G.I., Musin, R.Z., Fedorova, O.V., Rusinov, G.L., Zueva, M.N., Mordovskoi, G.G., and Tolstikov, A.G., *Pharm. Chem. J*., 2006, vol. 40, p. 473. doi 10.1007/s11094-006-0157-9
7. Al-Dhabi, N.A., Arasu, M.V., and Rejiniemon, T.S., *J. Evidence-Based Complementary Altern. Med*., 2015, vol. 2015, p. 164261. doi 10.1155/2015/164261
8. Andreeva, O.V., Sharipova, R.R., Strobykina, I.Yu., Kravchenko, M.A., Strobykina, A.S., Voloshina, A.D., Musin, R.Z., and Kataev, V.E., *Russ. J. Org. Chem*., 2015, vol. 51, p. 1324. doi 10.1134/S1070428015090201

9. Garifullin, B.F., Sharipova, R.R., Strobykina, I.Yu., Andreeva, O.V., Kravchenko, M.A., and Kataev, V.E., *Russ. J. Org. Chem*., 2015, vol. 51, p. 1488. doi 10.1134/S1070428015100231
10. Garifullin, B.F., Strobykina, I.Yu., Sharipova, R.R., Kravchenko, M.A., Andreeva, O.V., Bazanova, O.B., and Kataev, V.E., *Carbohydr. Res*., 2016, vol. 431, p. 15. doi 10.1016/j.carres.2016.05.007
11. Testai, L., Strobykina, I.Yu., Semenov, V.V., Semenova, M., Da Pozzo, E., Martelli, A., Citi, V., Martini, C., Breschi, M.C., Kataev, V.E., and Calderone, V., *Int. J. Mol. Sci*., 2017, vol. 18, p. 2056. doi 10.3390/ijms18102060
12. Liu, Y., Wang, T., Ling, Y., Bao, N., Shi, W., Chen, L., Sun, J., and Sun, J., *Chem. Biol. Drug Des*., 2017, vol. 90, p. 473. doi 10.1111/cbdd.12956
13. Khaybullin, R.N., Zhang, M., Fu, J., Liang, X., Li, T., Katritzky, A.R., Okunieff, P., and Qi, X., *Molecules*, 2014, vol. 19, p. 18676. doi 10.3390/molecules191118676
14. Wu, Y., Liu, C.-J., Liu, X., Dai, G.-F., Du, J.-Y., and Tao, J.-C., *Helv. Chim. Acta*, 2010, vol. 93, p. 2052. doi 10.1002/hlca.201000046
15. Huang, T.-J., Yang, C.L., Kuo, Y.C., Chang, Y.C., Yang, L.-M., Chou, B.-H., and Lin, S.-J., *Bioorg. Med. Chem*., 2015, vol. 23, p. 720. doi 10.1016/j.bmc.2014.12.064
16. Strobykina, I.Yu., Belenok, M.G., Semenova, M.N., Semenov, V.V., Babaev, V.M., Rizvanov, I.Kh., Mironov, V.F., and Kataev, V.E., *J. Nat. Prod*., 2015, vol. 78, p. 1300. doi 10.1021/acs.jnatprod.5b00124
17. Sharipova, R.R., Andreeva, O.V., Garifullin, B.F., Strobykina, I.Yu., Strobykina, A.S., Voloshina, A.D., Kravchenko, M.A., and Kataev, V.E., *Chem. Nat. Compd*., 2018, vol. 54, p. 92. doi 10.1007/s10600-018-2267-5
18. Strobykina, I.Yu., Garifullin, B.F., Sharipova, R.R., Voloshina, A.D., Strobykina, A.S., Dobrynin, A.B., and Kataev, V.E., *Chem. Nat. Compd*., 2017, vol. 53, p. 1011. doi 10.1007/s10600-017-2210-1
19. Strobykina, I.Yu., Andreeva, O.V., Garifullin, B.F., Sharipova, R.R., and Kataev, V.E., *Russ. J. Gen. Chem*., 2017, vol. 87, p. 579. doi 10.1134/S1070363217030331
20. Strobykina, I.Yu., Garifullin, B.F., Strobykina, A.S., Voloshina, A.D., Sharipova, R.R., and Kataev, V.E., *Russ. J. Gen. Chem*., 2017, vol. 87, p. 890. doi 10.1134/S1070363217030331
21. Sanki, A.K., Boucau, J., Srivastava, P., Adams, S.S., Ronning, D.R., and Sucheck, S.J., *Bioorg. Med. Chem*., 2008, vol. 16, p. 5672. doi 10.1016/j.bmc.2008.03.062
22. Ferrier, R.J. and Haines, S.R., *J. Chem. Soc., Perkin. Trans. 1*, 1984, p. 1689. doi 10.1039/P19840001689
23. Nishizono, N. and Nair, V., *Nucleosides, Nucleotides Nucleic Acids*, 2000, vol. 19, p. 283. doi 10.1080/15257770008033010
24. Podvalnyy, N.M., Sedinkin, S.L., Abronina, P.I., Zinin, A.I., Fedina, K.G., Torgov, V.I., and Kononov, L.O., *Carbohydr. Res*., 2011, vol. 346, p. 7. doi 10.1016/j.carres.2010.11.002
25. Ahiadorme, D.A., Podvalnyy, N.M., Orlova, A.V., Chizhov, A.O., and Kononov, L.O., *Russ. Chem. Bull., Int. Ed*., 2016, vol. 65, p. 2776. doi 10.1007/s11172-016-1654-y
26. Gao, M., Chen, Y., Tan, S., Reibenspies, J.H., and Zingaro, R.A., *Heteroatom Chem*., 2008, vol. 19, p. 199. doi 10.1002/hc.20388
27. Lopez, G., Nugier-Chauvin, C., Remond, C., and O'Donohue, M., *Carbohydr. Res*., 2007, vol. 342, p. 2202. doi 10.1016/j.carres.2007.06.001
28. Korochkina, M., Fontanella, M., Casnati, A., Arduini, A., Sansone, F., Ungaro, R., Latypov, Sh., Kataev, V., and Alfonsov, V., *Tetrahedron*, 2005, vol. 61, p. 5457. doi 10.1016/j.tet.2005.03.127
29. Aitken, A.A., Collet, C.J., and Mesher, Sh.T.E., *Synthesis*, 2012, vol. 44, p. 2515. doi 10.1055/s-0031-1290823