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Specific Features of Phase Transfer Catalytic Glycosylation of Aromatic Hydroxy Acids

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Abstract—Reactions of peracetylated α-*D*-glucosaminyl chloride with isomeric hydroxybenzoic and 1-hydroxy-2-naphthoic acids in a solid phase transfer system of potassium carbonate–acetonitrile were studied. It was found that the nature of carboxylic acids, lipophilicity of the phase transfer catalyst, and reaction temperatures affected the reaction composition and product yields. The *O*-β-glycosyl esters of *ortho*-hydroxyaromatic acids were first found to form anomeric 1,2-*cis* derivatives in the presence of potassium carbonate. The structures of the synthesized compounds were confirmed by ^{1}H NMR spectroscopy. As was shown in vivo experiments, the analgesic activities of glycosyl esters of salicylic acid and peracetylated 2-carboxyphenylglucosaminide were comparable with that of aspirin.

Keywords: analgesic activity, aromatic hydroxy acids, crown ether, glucosaminides, glycosyl ester, glycosylation, phase transfer catalysis

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INTRODUCTION

Selective modifications of polyfunctional aromatic compounds supporting the molecular design of biologically active compounds with carbohydrate residues have been extensively reported [1–5]. As was shown in some publications, aromatic compounds with hydroxy groups differing in acidity [6, 7] and capacity to chelating neighboring carbonyl groups [5] have different potency for glycosylation reactions. It was found that carbohydrate residues can be regioselectively introduced at any of the hydroxyl groups by varying reaction conditions, although in most cases the preparation of glycosides with a definite structure requires preliminary protection of other nucleophilic centers potentially capable of being involved in glycosylation reactions [8, 9].

In the synthesis of glycosyl esters of aromatic hydroxy acids the regioselective introduction of a carbohydrate residue at a carboxy group can be achieved smoothly [10, 11], whereas selective glycosylation of phenolic hydroxy groups is only possible after preliminary protection of the carboxylic function. Enzymatic glycosylation of salicylic acid resulted nearly solely in 2-glucosyloxybenzoic acid. In enzymatic reactions of 3- and 4-hydroxybenzoic acids, both isomeric 3- and 4-glycosylbenzoic acids and the corresponding glycosyl esters were formed [12, 13].

Since carbohydrate derivatives of salicylic acid and some other nonsteroid anti-inflammatory products are considered as potential prodrugs nearly lacking negative side effects related to this group of drugs [11, 17–19], the development of approaches to the synthesis of aromatic hydroxy carboxylic acids varied in the number of carbohydrate residues and the study of their biological activity are a topical task.

RESULTS AND DISCUSSION

On the continuation of the research of the PT catalytic synthesis of 1-*O*-derivatives of *N*-acetyl glucosamine [20–23] we studied the reaction of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-glucosaminyl chloride (**V**) with *o*-, *m*-, and *p*-benzoic and 1-hydroxy-2-naphtoic acids. The presence of two functional groups in the molecules of glycosyl acceptors substantially differing in the deprotonating potential formed the background for the selective involvement of a carboxy function into the reaction with α-*D*-glucosaminyl chloride (**V**) (figure).

Previously, we demonstrated that the maximal conversion of the glycosyl donor (**V**) to glycosyl esters can be achieved at an equimolar ratio of chloride (**V**), carboxylic acid, and anhydrous potassium carbonate in anhydrous acetonitrile in the presence of catalytic amounts of 15C5 [24]. This approach resulted in the glycosyl ester (**Ia**) in a yield of 69% without *O*-glycoside as a side product (Table 1, method ***A***). In addition to the target (**Ia**), the reaction mixture contained β- and α-acetates (**VI**) and (**VII**) (TLC control with the

Abbreviations: 15C5, 15-crown-5; PT, phase transfer; [3.3] DB18C6, [3.3]-dibenzo-18-crown-6, PTC, phase transfer catalysis.

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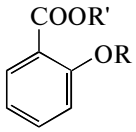
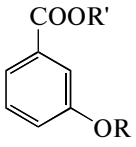


(I) R = R' = H
(Ia) R = H, R' = βG
(Ib) R = H, R' = αG
(Ic) R = R' = βG
(Id) R = αG, R' = βG
(Ie) R = Me, R' = H
(If) R = Me, R' = βG
(Ig) R = βG, R' = H



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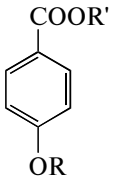
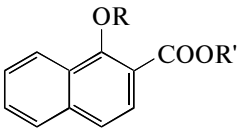
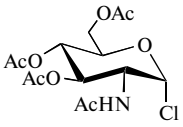
(IIa) R = H, R' = βG
(IIb) R = R' = βG



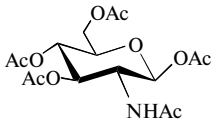
(III) R = R' = H
(IIIa) R = H, R' = βG
(IIIb) R = R' = βG



(IV) R = R' = H
(IVa) R = H, R' = βG
(IVb) R = H, R' = αG
(IVc) R = R' = βG



(V)



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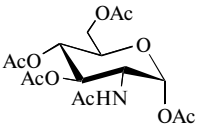

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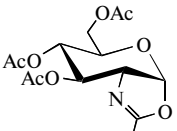
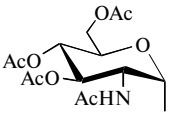
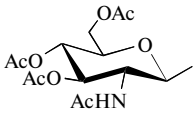


(VIII)



αG



βG

The structures of glycosyl donor **(V)**, substituted benzoic acids **(I)**–**(IV)**, (**Ie**, **g**), their carbohydrate-containing derivatives, and identified side products **(VI)**–**(VIII)**.

reference compounds), which we previously observed in phase transfer reactions [24]. In the absence of the PT catalyst the total conversion of glucosaminyl chloride **(V)** was completed in 6 h to give 40% of product **(I)** (Table 1, method ***B***). Thus, the use of 15C5 allowed a twofold reduction of the glucosaminylation time and an increase in the target product **(Ia)** yield by 20% if compared with the process in the absence of the catalyst.

The use of the base excess led to the results shown in Table 1, method ***C***. It was found that in addition to bisderivative **(Ic)**, side compounds **(VI)**, and **(VII)** and unspecified products of the carbohydrate destruction, the reaction mixture contained a compound that

Table 1. Conditions and results of phase transfer glucosaminylation of aromatic acids with α-chloride **(V)**

Method	*T*, °C	Chloride **(V)**, mmol	Glycosyl acceptor, mmol	Crown ester, 0.2 mmol	Base, mmol	Reaction time, h	Reaction products/yield, %	Side reaction products
A	22	1.10	**(I)**, 1.10	15C5	K_2CO_3, 1.10	3	**(Ia)**/69	**(VI)**, **(VII)**
B	22	1.10	**(I)**, 1.10	0	K_2CO_3, 1.10	6	**(Ia)**/40	**(VI)**, **(VII)**
C	22	1.10	**(I)**, 1.10	15C5	K_2CO_3, 6.05	3	**(Ic)**/8, **(Id)**/7	**(VI)**, **(VII)**
D	22	0.87	**(Ia)**, 0.87	15C5	K_2CO_3, 0.87	4	**(Ic)**/14, **(Id)**/6	**(VI)**, **(VII)**
E	22	0.55	**(Ig)**, 0.55	15C5	K_2CO_3, 0.55	5	**(Ic)**/58	**(VI)**, **(VII)**
F	22	0	**(Ia)**, 1.10	15C5	K_2CO_3, 1.10	2	**(Ib)**/41	**(VI)**, **(VII)**
G	22	0	**(Ia)**, 1.10	0	K_2CO_3, 1.10	2	**(Ib)**/51	**(VI)**, **(VII)**
A	22	1.10	**(II)**, 1.10	15C5	K_2CO_3, 1.10	30	**(IIa)**/49, **(IIb)**/15	**(VI)**, **(VII)**
H	50	1.10	**(III)**, 1.10	15C5	K_2CO_3, 1.10	6	**(IIIa)**/20, **(IIIb)**/22	**(VIII)**
I	22	1.10	**(III)**, 1.10	[3.3]DB 18K6	$KHCO_3$, 1.10	7	**(IIIa)**/38	**(VIII)**
A	22	1.10	**(IV)**, 1.10	15C5	K_2CO_3, 1.10	12	**(IVa)**/43, **(IVc)**/7	**(VI)**, **(VII)**
D	22	0.77	**(IVa)**, 0.77	15C5	K_2CO_3, 3.47	5	**(IVc)**/69	**(VI)**, **(VII)**
G	22	0	**(IVa)**, 1.10	0	K_2CO_3, 1.10	>10	**(IVb)**/27	**(VI)**, **(VII)**
A	22	1.10	**(Ie)**, 1.10	15C5	K_2CO_3, 1.10	3	**(If)**/67	**(VI)**, **(VII)**

Table 2. ^{1}H NMR spectral data of bisderivatives (**Ic**, **d**), (**IIb**), (**IIIb**), (**IVc**)

Protons	CS (ppm), multiplicity, and SSCC (J_{HH}, Hz)				
	(Id)	**(Ic)**	**(IIb)**	**(IIIb)**	**(IVc)**
H1 ($J_{1,2}$)	5.59d (8.4), 6.17d (3.2)	5.53d (8.8), 5.92d (8.8)	5.49d (8.4), 5.83d (8.8)	5.43d (9.2), 5.86d (8.8)	5.13d (8.4), 5.90d (8.8)
H2 ($J_{2,3}$)	4.18m	4.11m	4.18m	4.06m, 4.23m	4.15m
H3 ($J_{3,4}$)	5.28dd (2H) (9.6)	5.28dd (9.6), 5.25dd (9.6)	5.21dd (9.6), 5.23dd (9.2)	5.25dd (10.4), 5.27dd (10.4)	4.95dd (9.6), 5.27dd (10.0)
H4 ($J_{4,5}$)	4.97dd (9.6), 5.04dd (10.0)	4.93dd (10.0), 4.96dd (9.6)	4.93dd (9.6), 4.95dd (9.6)	4.94dd (10.0), 4.97dd (9.2)	4.81dd (8.8), 5.20dd (9.6)
H5 ($J_{5,6a}$; $J_{5,6b}$)	4.18m	4.11m	4.03m	4.15m, 4.34m	3.63ddd (2.0; 5.0), 4.06m
H6 (J_{qem})	4.18m	4.11m	4.03m	4.23m, 4.01m	3.78dd, 4.23dd (12.0), 4.12m (2H)
NHAc	1.72s, 1.81s	1.76s, 1.78s	1.73s, 1.77s	1.79s, 1.80s	1.86s, 1.88s
OAc	1.96s (9H), 1.99s, 2.01s, 2.02s	1.97s,1.98s, 2.00s, 2.02s, 2.01s (6H)	1.96s, 1.97s, 1.99s, 2.01s (9H)	1.97s, 1.99s, 2.00s (6H), 2.01s, 2.02s	1.95s, 1.96s, 1.98s, 1.99s, 2.02s, 2.04s
NH ($J_{NH,2}$)	8.00d (8.0), 8.01d (8.4)	7.95d (8.0), 8.06d (9.6)	8.03d (9.2), 8.08d (9.2)	8.10d (9.2), 8.14d (9.2)	8.28d (8.0), 8.36d (9.2)
CH_{arom}	7.22t, 7.39d, 7.64dd, 7.89d	7.13t, 7.28d, 7.59dd, 7.73d	7.15d (2H), 7.90d (2H)	7.32dd, 7.51d, 7.52s, 7.64d	7.54d, 7.60dd, 7.66dd, 7.89d, 7.95d, 8.10d

Note: The working frequency of 400 MHz; DMSO-d_6 as a solvent.

could not pertain to any of the known products of the α-chloride (**V**) conversion under PTC conditions according to the TLC analysis (Figure) [22, 24, 25]. Due to the presence of two doublets of anomeric protons at 6.17 and 5.59 ppm and *J* 3.2 Hz and 8.4 Hz respectively (Table 2), the structure of this compound was unambiguously defined as bisderivative (**Id**) with the α-configuration of the glycosyl ester and β-configuration of the glycosyl bonds (Figure). The formation of derivative (**Id**) may be explained by anomerization of the glycosyl ester (**Ia**) in the process of synthesis.

The substantial impact of side reactions led to low yields of compounds (**Ic**) and (**Id**) (8 and 7% respectively) (Table 1, method ***C***). An insignificant increase in the yield of product (**Ic**) to 14% was achieved by the reaction of the glycosyl ester (**Ia**) with α-chloride (**V**) in the presence of the equimolar amount of potassium carbonate. The yield of isomer (**Id**) remained nearly unchanged at 6% (Table 1). Thus, the formation of the α-anomer (**Id**) was a result of anomerization of the glycosyl ester (**Ia**) but not the pseudodisaccharide (**Ic**) (figure). To confirm this hypothesis, a mixture of glycosyl ester (**Ia**), potassium carbonate, and 15C5 (20 mol %) was stirred in anhydrous acetonitrile (Table 1, method ***F***) until anomerization of ester (**Ia**) was completed (2 h, TLC, ^{1}H NMR spectroscopy, Table 3). The yield of the α-anomer (**Ib**) was 41%. In addition, acetates (**VI**), (**VII**), and some unspecified products of carbohydrate destruction were formed. In the absence of the PT catalyst the process was also completed in 2 h to give 51% α-anomer (**Ib**) (Table 1, method ***G***). Similar procedures with compound (**Ic**) failed to give the product (**Id**). The use of an alternative approach, the synthesis of compound (**Ic**) from *o*-carboxyphenyl-β-*D*-glucosaminide (**Ig**) (Table 1, method ***E***), resulted in the only product (**Ic**) with the β-configuration of the anomeric center in both carbohydrate residues (Table 2).

The interaction of equimolar amounts of *m*-hydroxybenzoic acid (**II**), chloride (**V**), and the base in anhydrous acetonitrile in the presence of 20 mol % 15C5 for 30 min resulted in 49 and 15% of mono- and bisderivatives (**IIa**) and (**IIb**), respectively (Table 1, method ***A***). It is noteworthy that our attempt of the regioselective preparation of the glycosyl ester (**IIa**) failed. Also, we failed to synthesize the glycosyl ester of *p*-hydroxybenzoic acid (**IIIa**) under these conditions and could only observe small destruction of chloride (**V**). Derivatives (**IIIa**) and (**IIIb**) were obtained in yields of 20 and 22% when the reaction temperatures were increased to 50°C. This increase also supported the formation of oxazoline (**VIII**) (TLC control, the comparison with the reference compound) and some unidentified carbohydrate destruction products (Table 1, method ***H***). The regioselective synthesis

Table 3. ^{1}H NMR spectral data of glycosyl esters (**Ia**, **b**, **f**), (**IIa**), (**IIIa**), (**IVa, b**)

Protons	CS (ppm), multiplicity, and SSCC (J_{HH}, Hz)						
	(Ia)*	**(Ib)**	**(If)**	**(IIa)**	**(IIIa)**	**(IVa)**	**(IVb)**
H1 ($J_{1,2}$)	5.92d (8.4)	6.25d (3.2)	5.86d (8.4)	5.90d (8.8)	5.81d (8.8)	5.97d (8.4)	6.37d (3.2)
H2 ($J_{2,3}$)	4.12m	4.37ddd (9.8)	4.11ddd (8.8)	4.15ddd (9.6)	4.19m	4.25ddd (8.8)	4.44ddd (10.2)
H3 ($J_{3,4}$)	5.27dd (10.2)	5.35dd (8.8)	5.23dd (9.6)	5.23dd (9.6)	5.22dd (9.6)	5.29dd (8.8)	5.40dd (10.8)
H4 ($J_{4,5}$)	4.97dd (10.2)	5.06dd (9.2)	4.95dd (9.6)	4.96dd (10.0)	4.94dd (10.0)	4.99dd (10.0)	5.10dd (9.2)
H5 ($J_{5,6a}$; $J_{5,6b}$)	4.12m	4.28ddd (2.4; 4.0)	4.03m	4.12m	4.01m	4.11ddd (2.0; 4.0)	4.31ddd (2.0; 4.0)
H6 (J_{gem})	4.12m	4.02dd, 4.21dd (12.4)	4.03m	4.03dd, 4.23dd (12.0)	4.01m	4.01dd, 4.04dd (12.4)	4.03dd, 4.23dd (12.0)
NHAc	1.75s	1.79s	1.76s	1.74s	1.73s	1.76s	1.79s
OAc	1.96s, 2.00s (6H)	1.97s, 2.00s, 2.01s	1.96s, 2.00s, 2.02s	1.96s, 2.01s (6H)	1.96s, 2.00s (2H)	2.00s, 2.01s, 2.02s	1.99s, 2.00s, 2.02s
NH ($J_{NH,2}$)	8.09d, (9.3)	8.20d (8.4)	8.03d (9.6)	8.07d, (9.2)	8.02d (9.6)	8.32d (8.0)	8.34d (8.4)
CH_{arom}	6.96dd, 7.01d, 7.55dd, 7.68d	7.01d, 7.55m, 7.94d, 7.96d	7.02dd, 7.15d, 7.58dd, 7.67d	7.37s, 7.33d (2H), 7.07dd	6.84d (2H), 7.78d (2H)	7.41d, 7.59dd, 7.69dd, 7.70d, 7.88d, 8.03d	7.56d, 7.64dd, 7.75 dd, 7.97d, 7.99d, 8.34d
OH	10.19s	10.40s	–	9.97s	10.46s	11.50s	11.56s
$-OCH_3$	–	–	3.83s	–	–	–	–

* The working frequency of 300 MHz; for the other compounds, 400 MHz.

of the glycosyl ester (**IIIa**) was performed in the presence of [3.3]DB18C6, a higher lypophilic macrocyclic ester, and potassium hydrocarbonate. Under these conditions the substrate (**V**) was converted to the product (**IIIa**) in a yield of 38% and oxazoline (**VIII**) (Table 1, method ***J***). It was found that in the reactions of chloride (**V**) with either *meta*- or *para*-hydroxybenzoic acids (**II**) or (**III**) the anomerzation of the corresponding glycosyl esters (**IIa**) or (**IIIa**) did not take place.

No regioselective formation of glycosyl esters was observed in the reaction of chloride (**V**) and 1-hydroxy-2-naphtoic acid (**IV**), whose functional groups are located similarly to that of salicylic acid (**I**) (Table 1, method ***A***). Together with glucopyranose (**IVa**), the bisderivative (**IVc**) was formed (43 and 7% respectively). The yield of the derivative (**IVc**) was increased to 69% when the glycosyl ester (**IVa**) was used as a glycosyl acceptor (Table 1, method ***D***). No formation of a bisderivative with the α-configuration of the glycosyl ester bond was observed under these conditions (method ***D***) even in the presence of the base excess. However, keeping the glycosyl ester (**IVa**) in dry acetonitrile in the presence of potassium carbonate (Table 1, method ***G***) provided 27% of ester (**IVb**). Its formation was proved by ^{1}H NMR spectral data (Table 4). The conversion of ester (**IVa**) to the α-anomer (**IVb**) was incomplete.

The anomerization was only observed for acids (**I**) and (**IV**) with the *ortho*-location of functional groups, which supported the involvement of the proton of the phenolic hydroxy group in the anomerization process. This was confirmed experimentally using the preliminary prepared glycosyl ester of 2-methoxybenzoic acid (**If**), whose stirring in acetonitrile in the presence of potassium carbonate did not result in anomerization.

The structures of the synthesized compounds (**Ia**–**d**, **f**), (**IIa**, **b**)–(**IVa**, **b**) were confirmed by ^{1}H NMR spectroscopy (Tables 2 and 3). A characteristic feature of the ^{1}H NMR spectra of glycosyl esters (**Ia**, **b**), (**IIa**), (**IIIa**), and (**IVa**, **b**) was the presence of a phenolic hydroxy group singlet at 9.97–11.50 ppm and a significant downfield shift of the anomeric proton doublet (δ 5.81–6.25 ppm), which agrees well with the previous data [24]. Values of $J_{1,2}$ in glycosyl esters (**Ia**)–(**IVa**)

Table 4. Physicochemical constants of compounds (**Ia**–**d**, **f**)–(**IVa**–**c**)

Compound	mp, °C	$[\alpha]_{546}$ (*c* 1.0; $CHCl_3$)	Compound	mp, °C	$[\alpha]_{546}$ (*c* 1.0; $CHCl_3$)
(Ia)	140–142	–50°	**(IIb)**	192–193	–25°
(Ib)	155–157	+231°	**(IIIa)**	172–174	–44°
(Ic)	130–134	–38°	**(IIIb)**	193–194	–33°
(Id)	209–211	–34°	**(IVa)**	148–149	+8°
(If)	amorph.	–21°	**(IVb)**	amorph.	+181°
(IIa)	160–161	–63°	**(IVc)**	174–176	–58°

were observed in a range of 8.4–8.8 ppm, which is common for *O*-β-glucosaminides. For glycosyl esters (**Ib**) and (**IVb**) the *J* value of 3.2 Hz can be explained by a 1,2-*cis* diaxial localization of carbohydrate protons. The absence of the resonance of the phenolic hydroxy group and duplication of the resonances of carbohydrate backbone protons relative to aglycon resonances was characteristic for bisderivatives (**Ic**, **d**), (**IIb**), (**IIIb**) and (**IVc**). In the ^{1}H NMR spectra of derivatives (**Ic**), (**IIb**), (**IIIb**), and (**IVc**) the *J* value of the anomeric proton doublet of 8.4–8.8 Hz evidenced the β-configuration of glycosyl and glycoside bonds. Chemical shifts of the resonances of carbohydrate backbone protons and aglycon resonances of mono- and biscarbohydrate derivatives corresponded to those found in previous studies [20–25].

With the goal of the assessing the impact of *N*-acetylglucosamine residues in the molecule of salicylic acid on the analgesic activity we compared derivatives (**Ia**) and (**Ic**) with aspirin as a reference in the test for the pain threshold [26] on white outbred male rats. We showed that the analgesic activities of these compounds were comparable with that of aspirin. The results of these experiments will be published later.

EXPERIMENTAL

Melting points were measured on a PTP device in open glass capillaries at a heating rate of 4°C/min. Optical rotation was measured on a Polamat-A polarimeter at 20–22°C.

The analysis of compositions of the reaction mixtures, the purity of the synthesized compounds as well as the reaction monitoring were performed by TLC on Sorbfil-AFV-UV plates (Sorbpolymer, Russia). The chromatograms were developed in 40 : 1 chloroform–ethanol (A), and 15 : 1 chloroform–ethanol (B) systems. The compounds were detected with 5% sulfuric acid in propan-2-ol at 200–300°C or by UV irradiation at a wavelength of 254 nm. The compounds were isolated by column chromatography on Kieselgel 60 (0.063–0.200 mm).

^{1}H NMR spectra (ppm, δ scale, *J*, Hz) were recorded on Varian VXR-300 (300 MHz) and Varian Mercury-400 (400 MHz) spectrometers with Me_4Si as an internal standard and DMSO-d_6 as a solvent.

15-Crown-5 was purchased from Merck (Germany), [3.3]DB18C6 of at least 98% purity, from Bogatskii Physicochemical Institute, National Academy of Science of Ukraine, Odessa, *N*-acetylglucosamine, from Acros (Belgium), and *o*-, *m*-, *p*-benzoic acids (**I**)–(**III**) and 1-hydroxynaphtoic acid (**IV**), from Reachim (Russia).

Acetonitrile was refluxed with phosphorus oxide (**V**), fractioned, refluxed with freshly calcined potassium carbonate, distilled, and the distillate was fractionated using a Vigreux column. Dry K_2CO_3 was obtained by calcination for 5h at 340–360°C followed by grinding and fractionating with 140 μm sieves. The fraction with the particle size of 140 μm and less was used in PT reactions.

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-glucosaminyl chloride (**V**) and 2-carboxyphenyl-2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranoside (**Ig**) were prepared as described in [28] and [29], respectively.

A general procedure of glucosaminylation. A mixture of α-chloride (**V**) (1.10 mmol), hydroxyaromatic acids (**I**)–(**IV**) or (**Ie**, **g**) (1.10 mmol), compounds (1.10 mmol) or a base (6.02 mmol or 1.10 mmol), and crown ether (0.22 mmol) in anhydrous acetonitrile (12 mL) was stirred at 20–22°C or 50°C up to a full conversion of the glycosyl donor (TLC, system A) (Table 1). The solid phase was removed by filtration, the residue was washed on the filter with acetonitrile (2 × 5 mL), and the solvent was evaporated in vacuum. The reaction products (**Ia**, **c**–**d**, **f**), (**IIa**, **b**), (**IIIa**, **b**), and (**IVa**, **c**) were obtained by column chromatography in a gradient manner using the following systems: 100 : 1 toluene–propan-2-ol → 30 : 1 toluene–propan-2-ol → 100 : 1 chloroform–propan-2-ol 1 → and 25 : 1 chloroform–propan-2-ol.

A general procedure of anomerizarion. A mixture of glycosyl ester (**Ia**) or (**IVa**) (0.55 mmol), anhydrous potassium carbonate (0.55 mmol), 15C5 (0.22 mmol) or without it in anhydrous acetonitrile (12 mL) was stirred at 20–22°C or 50°C up to a full conversion of the starting ester (TLC, system A). The reaction prod-

ucts (**Ib**) and (**IVb**) were isolated as described above for glucosaminylation reactions (Table 1).

A general procedure of glycosylation. A mixture of glycosyl ester (**Ia**), (**IVa**), or β-*D*-glucopyranoside (**Ig**) (0.87 mmol), α-chloride (**V**) (0.87 mmol), anhydrous potassium carbonate (0.87 mmol), and 15C5 (0.17 mmol) in anhydrous acetonitrile (10 mL) was stirred up to a full conversion of the glycosyl donor (TLC, system B) (Table 1). The reaction products (**Ic**, **d**) and (**IVc**) were isolated as described above for glucosaminylation reactions (Table 1).

REFERENCES

1. Hongu, M., Saito, K., and Tsujihara, K., *Synth. Commun.*, 1999, vol. 29, pp. 2775–2781.
2. Wang, Y., Li, L., Wang, Q., and Li, Yu., *Synth. Commun.*, 2001, vol. 31, pp. 3423–3427.
3. Rothermel, J. and Faillard, H., *Carbohydr. Res.*, 1990, vol. 196, pp. 29–40.
4. Ngameni, B., Patnam, R., Sonna, P., Ngadjui, B.T., Roy, R., and Abegaz, B.M., *ARKIVOC*, 2008, vol. 6, pp. 152–159. www.arkat-usa.org
5. Grabley, S., Garies, M., Bockers, W., and Thiem, J., *Synthesis*, 1992, vol. 27, pp. 1078–1080.
6. Demetzos, C., Skaltsounis, A.-L., Tillequin, F., and Koch, M., *Carbohydr. Res.*, 1990, vol. 207, pp. 131–137.
7. Du, Y., Wei, G., and Linhardt, R.J., *J. Org. Chem.*, 2004, vol. 69, pp. 2206–2209.
8. Alluis, B. and Dangles, O., *Helvetica Chimica Acta*, 2001, vol. 84, pp. 1133–1156.
9. Du, Y., Wei, G., and Linhardt, R.J., *Tetrahedron Lett.*, 2003, vol. 44, pp. 6887–6890.
10. Borowiecka, J. and Michalska, M., *Synthesis*, 1994, no. 7, pp. 709–713.
11. Borowiecka, J. and Stańczak, A., *IlFarmaco*, 2001, vol. 56, pp. 257–262.
12. Tanaka, S., Hayakawa, K., Umetani, Y., and Tabata, M., *Phytochemistry*, 1990, vol. 29, pp. 1555–1558.
13. Kawano, T., Tanaka, S., Kadono, T., and Muto, S., *Z. Naturforsc.*, 2004, vol. 59c, pp. 684–692.
14. Strachan, R.G., Ruyle, W.V., Shen, T.Y., and Hirschmann, R., *J. Org. Chem.*, 1966, vol. 31, pp. 507–509.
15. Hennig, J., Malamy, J., Grynkiewicz, G., Indulski, J., and Klessig, D.F., *Plant J.*, 1993, vol. 4, pp. 593–600.
16. Xue, L., Sun, G., and Gao, J., *Huaxuefongbao = Chemistry*, 1994, no. 1, pp. 30–32. (Ros. Chem. Zh., 1994, 24E18).
17. Hanessian, S., Mascitti, V., Lu, P.-P., and Ishida, H., *Synthesis*, 2002, no. 14, pp. 1959–1968.
18. Samczewska, G. and Borowiecka, J., *Acta Poloniae Pharm. Drug Res.*, 1999, vol. 56, pp. 361–366.
19. Grynkiewicz, G., Szeja, W., and Boryski, J., *Acta Poloniae Pharm. Drug Res.*, 2008, vol. 65, pp. 655–676.
20. Kuryanov, V.O., Chupakhina, T.A., Zemlyakov, A.E., Kotlyar, S.A., Kamalov, G.L., and Chirva, V.Ya., *Russ. J. Bioorg. Chem.,* 2001, vol. 27, pp. 385–389.
21. Chupakhina, T.A., Kur'yanov, V.O., Chirva, V.Ya., Grigorash, R.Ya., Kotlyar, S.A., and Kamalov, G.L., *Russ. J. Bioorg. Chem.*, 2004, vol. 30, pp. 301–303.
22. Kuryanov, V.O., Katsev, A.M., Chupakhina, T.A., and Chirva, V.Ya., *Zh. Org. Farm. Khim.*, 2009, vol. 7, pp. 30–40.
23. Kuryanov, V.O., Chupakhina, T.A., Shapovalova, A.A., Katsev, A.M., and Chirva, V.Ya., *Russ. J. Bioorg. Chem.*, 2011, vol. 37, pp. 231–239.
24. Kuryanov, V.O., Chupakhina, T.A., and Chirva, V.Ya., *Zh. Org. Farm. Khim.*, 2009, vol. 7, pp. 57–63.
25. Kuryanov, V.O., Chupakhina, T.A., Shishkin, O.V., Shishhkina, S.V., and Chirva, V.Ya., *Russ. J. Bioorg. Chem.*, 2008, vol. 34, pp. 730–738.
26. Caram, S.M. and Shen, K.F., *Brain Res.*, 2001, vol. 888, pp. 75–82.
27. Mashkovskii, M.D., *Lekarstvennye sredstva. Posobie dlya vrachei*: (Drugs: Manual for Doctors), Moscow: Novaya volna, 2002.
28. *Metody issledovaniya uglevodov* (Methods of Carbohydrate Research), Khorlin, A.Ya., Ed., Moscow: Mir, 1975, pp. 221–224.
29. Kuryanov, V.O., Chupakhina, T.A., Kotlyar, S.A., and Chirva, V.Ya., *Zh. Org. Farm. Khim.*, 2007, vol. 5, pp. 44–48.

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