ISSN 1068-1620, Russian Journal of Bioorganic Chemistry, 2006, Vol. 32, No. 4, pp. 389–399. © Pleiades Publishing, Inc., 2006.
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The Study of the Reaction of Terminated Oligomerization in the Synthesis of Oligo-(β1-6)-Glucosamines

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Received December 28, 2005; in final form, January 12, 2006

Abstract—The applicability of terminated oligomerization to the synthesis of oligo-(β1-6)-glucosamines, fragments of the intercellular polysaccharide adhesin of staphylococci, was studied. The reactions of terminated oligomerization were carried out with mono-, di-, and trisaccharide monomers and *N*-protected aminopropanol; and spacered mono- and disaccharides as terminating molecules were also attempted. The primary formation of cyclic products of monomer intramolecular glycosylation was observed in almost all the reactions. Only the experiments with the monomer based on the disaccharide bromide under the conditions of the Helferich reaction led to reduced yields (30%) of the cyclic products. However, even in this case, the desired terminated oligosaccharides were generated in approximately 10% yield and mainly were the products of single glycosylation of the terminator by the monomer. These experiments allow the conclusion that, under the examined conditions, the reaction of terminated oligomerization could not result in the synthesis of oligoglucosamines with a high molecular mass.

DOI: 10.1134/S1068162006040108

Key words: cyclic oligosaccharides, oligo-(β1-6)-glucosamines, terminated oligomerization

INTRODUCTION

Staphylococcus aureus is one of the most frequently revealed pathogenic bacteria. It is known to cause a large number of diseases with a high lethality.[2] For example, it is the cause of diseases of the patients with medical implants, when the implant surfaces are colonized by *S. aureus* that covers them with adhesive biofilms, mainly consisting of poly-(β1–6)-*N*-acetylglucosamine [1]. Immunoassays suggest that the partially *N*-deacetylated analogues of this polysaccharide can induce the production of protective antibodies and, hence, offer promise as a basis for the design of antistaphylococcal vaccines. Synthetic oligo-(β1–6)-glucosamines with *N*-acetyl groups in the predetermined glucosamine residues are necessary for the elucidation of structure of the epitopes responsible for the production of protective antibodies.

Only several articles concerning the synthesis of oligo-(β1–6)-glucosamines have been published up to now. Various approaches, such as solid phase synthesis [2], multicomponent coupling using polymeric supports [3], polymerization of 1,6-anhydro derivatives [4], and block synthesis [5–7] were used. Some of the approaches resulted in oligosaccharides (up to nonasaccharides) in appropriate yields, but the oligosaccharides were mostly obtained in protected form rather than as deprotected derivatives necessary for biomedical studies. None of the published studies demonstrated the methods for the synthesis of spacered or labeled compounds for biological tests in vivo and nobody of the authors reported any immunological tests using these compounds.

RESULTS AND DISCUSSION

Investigation of a possibility of obtaining the series of oligomer homologues of the general formula [*D*-GlcN(β1–6)]$_n$-O(CH$_2$)$_3$NH$_2$ containing up to ten monosaccharide residues and bearing either only free, or *N*-acetylated amino groups using the reaction of terminated oligomerization was the first stage of our study. This reaction consists in the oligomerization of a bifunctional monomer in the presence of a monofunctional terminator, which is fixed at the reducing end of the growing oligosaccharide chain. A possibility of synthesis of homo- and block oligosaccharides through the reaction of terminated oligomerization of tritylated 1,2-*O*-cyanoethylidene derivatives of mono- and oligosaccharides had earlier been demonstrated [8, 9]. The results proved that the monomer–terminator ratio in a range from 10 : 1 to 5 : 1 gives a possibility to obtain

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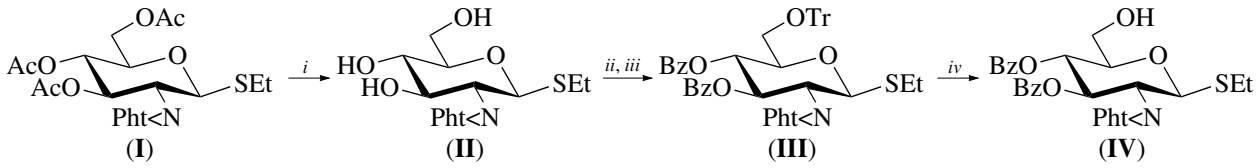
[2] Abbreviations: DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; Fmoc, fluorenylmethoxycarbonyl; NIS, *N*-iodosuccinimide; and TfOH, trifluoromethanesulfonic acid.



Reagents: (*i*) AcCl/MeOH, CH_2Cl_2; (*ii*) TrCl/pyridine; (*iii*) BzCl/pyridine; (*iv*) 90% aqueous CF_3COOH/CH_2Cl_2.

Scheme 1.

products with 10–11 monomeric units in approximately 40% yield [8]. The use of terminating residue allows the obtaining of oligosaccharides with a particular moiety at the reducing end, which, in our case, would lead to a series of spacered oligosaccharides necessary for the further synthesis of conjugates.

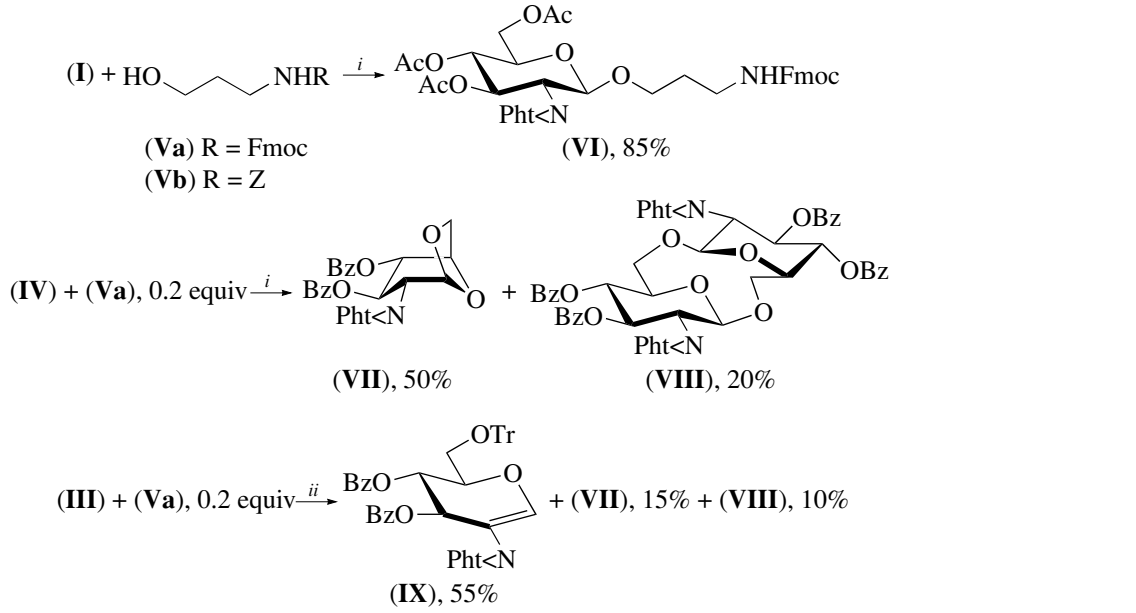
The first step was the synthesis of thioglycoside (**IV**) as a monomeric block (Scheme 1). Thioglycoside (**I**) [10] was deacetylated to triol (**II**) [11], which was then tritylated and benzoylated to get (**III**). Detritylation of (**III**) with trifluoroacetic acid in dichloromethane resulted in the target block (**IV**). The protective groups were chosen taking into account the effectiveness of their introduction and removal, their stability under the glycosylation conditions, and their ability to provide the necessary stereoselectivity of formation of *trans*-(β1 ⟶ 6)-glycosidic bonds. Benzoyl groups were chosen as the permanent protective groups for OH functions at C3 and C4, as they are not susceptible to migration unlike acetyl groups [12]. 3-Aminopropanol derivative (**Va**) was chosen as a terminating agent, since its *N*-protective group can be selectively removed, which is necessary for the isolation of the terminated products and would allow the further acylation of the spacer amino group. The monomer–terminator ratio was 5 : 1 in all experiments.

The model glycosylation reaction of terminator (**Va**) with thioglycoside (**I**) results in (*N*-Fmoc)aminopropyl glycoside (**VI**) in 85% yield. However, 1,6-anhydro derivative (**VII**) obtained in 50% yield turned out to be the main product of the terminated oligomerization of thioglycoside (**IV**) in the presence of terminator (**Va**) (Scheme 2). Cyclic disaccharide (**VIII**) (yield 20%) was another reaction product. Note that the pyranose ring in (**VII**) has a close to boat conformation, which follows from the coupling constants in its ^{1}H NMR spectrum ($J_{1,2} = 0$, $J_{2,3} = 9.2$, $J_{3,4} = 8.1$, $J_{4,5} = 0$, and $J_{C1,H3} = J_{C5,H3} = 1.5$). This conformation of (**VII**) seems to be stable because of equatorial positions of the bulky substituents at C2, C3, and C4 of the pyranose ring.

We presumed that the formation of 1,6-anhydro derivative (**VII**) can result from the spatial drawing together of C1 atom and hydroxy group at C6 in monomer (**IV**). Therefore, the next step was the oligomerization of (**III**) containing the trityl group (Scheme 2), which is known not to preclude glycosylation, but can create a steric barrier for intramolecular cyclization. In this case, the reaction resulted in the preferable formation of glycal (**IX**) along with cyclic products (**VII**) and (**VIII**).

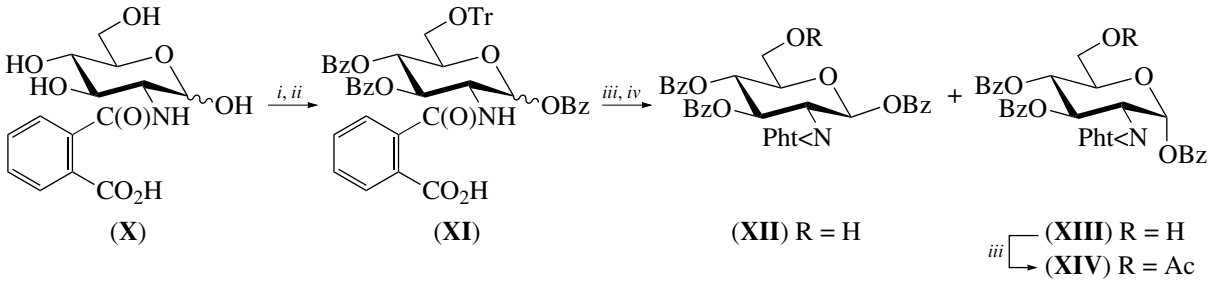
We hypothesized that the disaccharide dimer should be less prone to cyclization, which would enable obtaining the desired oligomeric products. The synthesis of monomeric blocks used in the preparation of disaccharides (**XVII**) and (**XVIII**) (see Scheme 4) is given in Scheme 3. The glucosamine derivative (**X**) containing *N*-(2-carboxy)benzoyl group was successively tritylated and benzoylated to the anomeric mixture (**XI**). The closure of the phthalimide cycle by treatment with acetic anhydride in pyridine under heating [13] and subsequent removal of trityl group resulted in a mixture of anomeric benzoates (**XII**) and (**XIII**). Individual α-isomer (**XIII**) and β-isomer (**XII**) were isolated by column chromatography. Acetylation of hydroxy derivative (**XIII**) led to 6-acetate (**XIV**). Benzoate (**XIV**) was converted into bromide (**XV**), which was put into the reaction of orthogonal glycosylation with acceptor (**IV**) to give disaccharide (**XVI**) (Scheme 4). The selective removal of acetyl group from (**XVI**) by acidic methanolysis [11] resulted in 6'-OH derivative (**XVII**). The treatment of thioglycoside (**XVII**) with bromine in dichloromethane resulted in bromide (**XVIII**).

The resulting monomers (**XVII**) and (**XVIII**) and terminator (**Va**) were used in a series of reactions of terminated oligomerization, in which we varied monomer concentration, temperature, solvent, leaving group, and promoting system (Scheme 5). All the reactions with thioglycoside (**XVII**) and bromide (**XVIII**) in the presence of silver triflate resulted in cyclic product (**VIII**) in almost quantitative yield. Only in the case of oligomerization of bromide (**XVIII**) under the conditions of the Helferich reaction, this compound was not the main reaction product. It should be noted that previously the same cyclic glucose derivatives had been reported to be also generated upon oligomerization of 6-*O*-(2,3,4-tri-*O*-acetyl-β-*D*-glucopyranosyl)-2,3,4-tri-*O*-acetyl-α-*D*-glucopyranosyl bromide in the presence of mercury salts; however, the yield of cyclic product was only 10% [14].



Reagents: (*i*) NIS, TfOH/CH_2Cl_2, molecular sieves 4 Å; (*ii*) MeOTf/CH_2Cl_2, molecular sieves 4 Å.

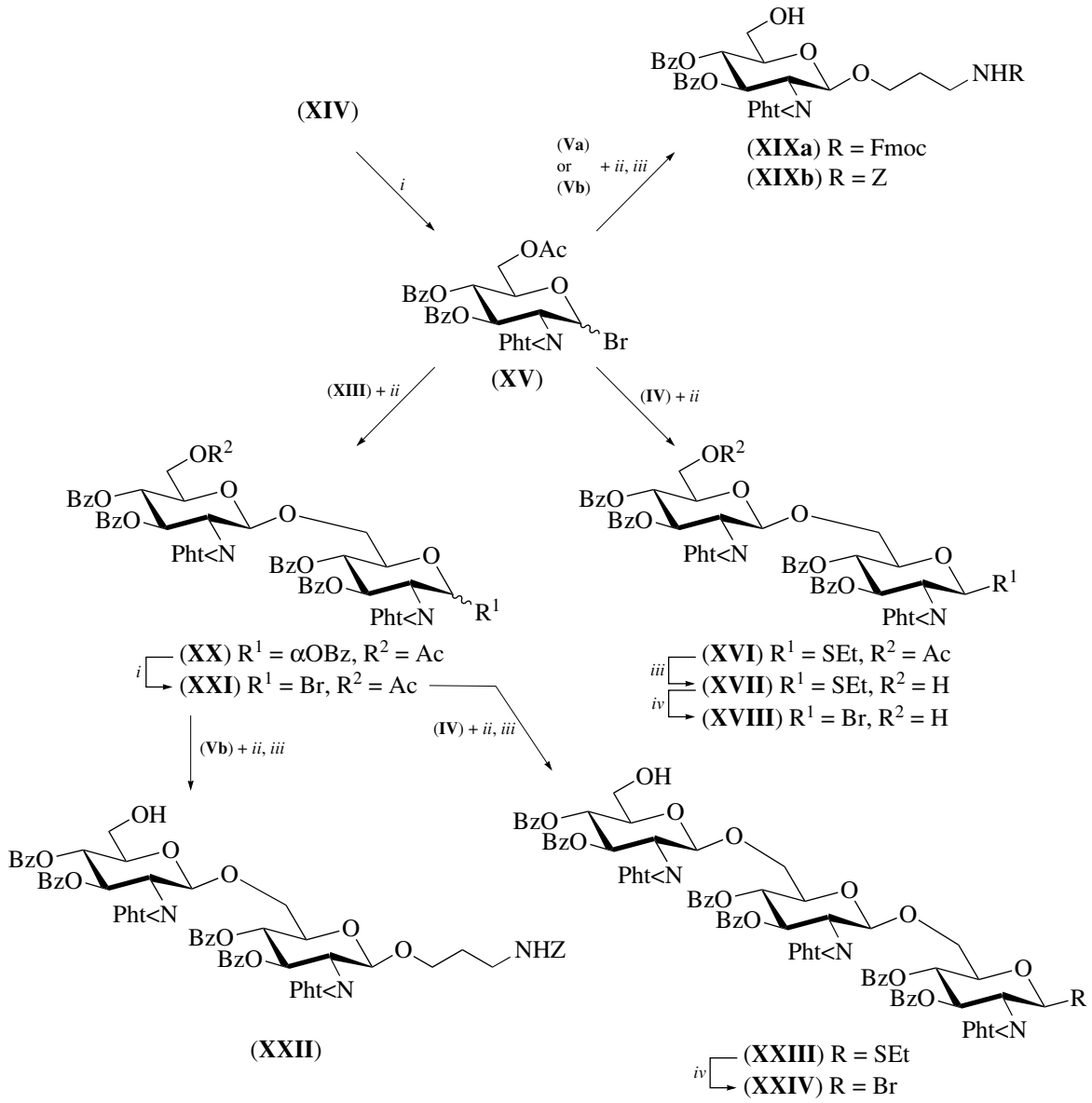
Scheme 2.



Reagents: (*i*) TrCl/pyridine; (*ii*) BzCl/pyridine; (*iii*) Ac_2O/pyridine; *(iv)* 90% aqueous CF_3COOH/CH_2Cl_2.

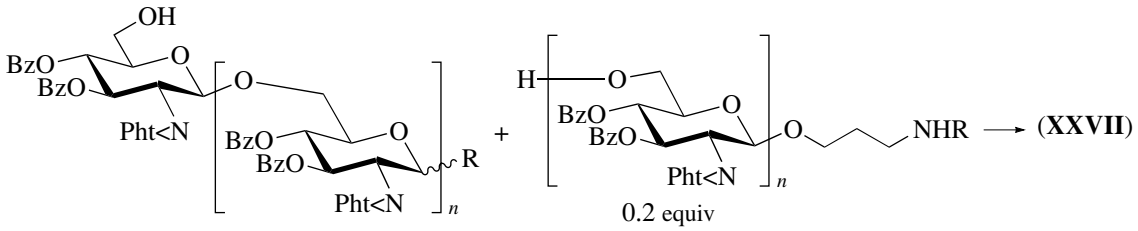
Scheme 3.

The oligomers obtained by (**XVIII**) + (**Va**) oligomerization in the presence of mercury salts were analyzed as follows. First, cyclic product (**VIII**) was separated by chromatography on silica gel. The remaining mixture containing terminated products (**XXV**) was treated to selectively remove the *N*-protective group from the aminopropyl spacer moiety. In this case, we did not use the classic procedure for the removal of Fmoc protective group, as it implies the use of an excess of such basic amines as piperidine and morpholine [15] and the resulting mixture of amines should complicate the subsequent ion exchange chromatography. The Fmoc protective group was removed in the presence of a catalytic amount of DBU and the excess of ethyl mercaptan necessary for the fixation of fulvene generated [16]. We met with difficulties in controlling the proceeding of this reaction in the case of the mixture of oligomers. Therefore, we have proceeded later to the use of *Z*-protected terminators. This has not caused any changes in their reactivity and the yields of the oligomerization products (see the table). Terminated oligosaccharides with the unprotected amino function in the aglycone (**XXVI**) were separated from the nonterminated products by ion exchange chromatography on Amberlyst 15 cation exchange resin. The mixture was then subjected to exhausting hydrazinolysis with the formation of totally deprotected spacered oligosaccharides (**XXVII**), which were then separated by gel chromatography.



Reagents: (*i*) HBr/AcOH, CH_2Cl_2; (*ii*) $HgBr_2$, $Hg(CN)_2/CH_3CN$; (*iii*) AcCl/MeOH, CH_2Cl_2; (*iv*) Br_2/CH_2Cl_2.

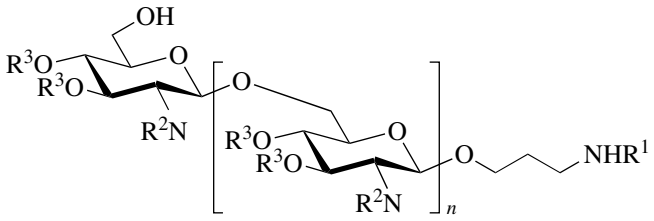
Scheme 4.



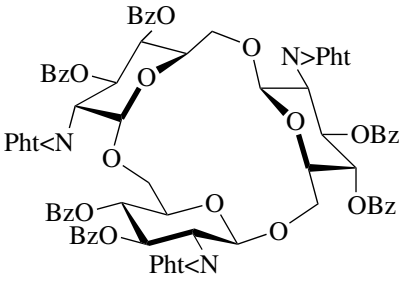
(**XVIII**) *n* = 1, R = Br
(**XXIII**) *n* = 2, R = SEt
(**XXIV**) *n* = 2, R = Br

(**Va**) *n* = 0, R = Fmoc
(**XIXa**) *n* = 1, R = Fmoc
(**XIXb**) *n* = 1, R = Z
(**XXII**) *n* = 2, R = Z

Scheme 5. Terminated oligomerization involving monomers and terminators of various lengths. The results are given in table.



(**XXV**) R^1 = Fmoc, R^2 = Pht<, R^3 = Bz, n = 1–4
(**XXVI**) R^1 = H, R^2 = Pht<, R^3 = Bz, n = 1–4
(**XXVII**) R^1 = H, R^2 = H_2, R^3 = H, n = 1–4



(**XXVIII**)

The experiment with bromide (**XVIII**) and Fmoc-substituted aminopropanol (**Va**) was analyzed according to the above scheme; the yield of terminated oligosaccharides was 10% (the table, experiment no. 1). Gel chromatography helped obtain the only spacered disaccharide (**XXVII**, n = 1). Such a low involving of the terminator in the reaction is likely the result of different reactivity of the hydroxy groups in the terminator and monomer. To adjust the reactivities of the acceptor hydroxy group of the terminating molecule and that of the monomer hydroxy group closer to one another, we passed to the use of terminators based on monosaccharides (**XIXa**) and (**XIXb**). The model reaction between disaccharide (**XXI**) and terminator (**XIXa**) led to the formation of the desired trisaccharide in 85% yield (not described). During the oligomerization (table, experiment no. 2), the yield of the terminated products was 12%, with 50% of terminator (**XIXa**) taken in the reaction being isolated from the reaction mixture in intact form. Monomer (**XVIII**) was added in 1-equiv portions to the terminator at regular intervals sufficient for complete expenditure of monomeric bromide (**XVIII**) in order to increase the terminator conversion (table, experiment no. 3). In this case, conversion of the terminator increased to 75% and the yield of dominating terminated oligomer (**XXII**, n = 2) was 15% (table, experiment no. 3). Therefore, we followed just the same order of the addition of the reagents in the further experiments.

The further elongation of the terminating residue up to disaccharide (**XXII**) did not result in any change in the yield of terminated oligosaccharides (table, experiment no. 5). The majority of experiments resulted in the formation of products of single glycosylation of the terminator with the monomer in low yields. Only in some cases, negligible amounts of the product of double glycosylation were detected among the isolated terminated oligomers by mass spectrometry.

The experiments with trisaccharide monomers (**XXIII**) and (**XXIV**) and terminator (**XXII**) (table, experiment nos. 6 and 7) were also carried out. The yield of cyclic trisaccharide (**XXVIII**) was 95% upon oligomerization of thioethyl glycoside (**XXIII**) and 50% in the case of bromide (**XXIV**). Previously, the only one example of the synthesis of similar (β1–6)-linked cyclic triglucoside obtained by cyclization of the corresponding peracetylated bromide was reported; however, the yield of this reaction after optimization did not exceed 20% [17]. It is possible that a higher tendency of trisaccharide (**XXIV**) for cyclization as compared with disaccharide (**XVIII**) can be explained by a much less tension in the cyclic trisaccharide, which makes it possible for monosaccharide fragments to occur in the undistorted minimal energy chair conformation as follows from the coupling constants ($J_{1,2}$ = 8.2; $J_{3,2} = J_{3,4}$ = 10.2; and $J_{4,5}$ = 9.5). In the case of the cyclic disaccharide, the values of coupling constants ($J_{1,2}$ = 4.2; $J_{3,2} = J_{3,4}$ = 10.5; and $J_{4,5}$ = 6.5) correspond to the distorted conformation of the ring close to the twist conformation. These data are in agreement with the results obtained earlier for the similar derivatives of glucose [17].

The results of terminated oligomerization reactions involving monomers and terminators of various lengths

Experiment no.	Monomer	Terminator	Reaction products (yield, %)
1	(**XVIII**)*	(**Va**)	(**VIII**) (30), (**XXVII**, n = 1) (10)
2	(**XVIII**)*	(**XIXa**)	(**VIII**) (30), (**XXVII**, n = 2) (12)
3	(**XVIII**)**	(**XIXa**)	(**VIII**) (25), (**XXVII**, n = 2) (15), (**XXVII**, n = 4) (<1%)
4	(**XVIII**)**	(**XIXb**)	(**VIII**) (25), (**XXVII**, n = 2) (12), (**XXVII**, n = 4)
5	(**XVIII**)**	(**XXII**)	(**VIII**) (25), (**XXVII**, n = 3) (14)
6	(**XXIII**)**	(**XXII**)	(**XXVIII**) (95)
7	(**XXIV**)**	(**XXII**)	(**XXVIII**) (50)

* The single addition of the monomer.
** The monomer was added in five portions.

Thus, under the conditions, the reaction of terminated oligomerization does not allow obtaining oligoglucosamines with a rather high molecular mass. Therefore, the gradient elongation of the oligoglucosamine chain, which we plan to realize in future, seems to be more promising.

EXPERIMENTAL

We used reagents from Fluka and Acros. Mass spectra were registered on a Finnigan LCQ mass spectrometer at electrospray ionization. The procedures for the purification of solvents and the conditions for the registration of NMR spectra (for solutions in $CDCl_3$) and measurement of coupling constants were similar to those reported in [18]. The values of optical rotation of the compounds obtained were measured on a JASCO DIP-360 (Japan) digital polarimeter in chloroform at 26–30°C. Silica gel 60 F_{254} precoated plates (Merck) were used for TLC. Spots were visualized by spraying with 10% orthophosphoric acid in ethanol and subsequent heating at ~150°C. Column chromatography was carried out on silica gel 60–200 μm (Fluka).

Ethyl 3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-1-thio-6-*O*-trityl-β-*D*-glucopyranoside (III). Trityl chloride (3.47 g, 12.6 mmol) was added to a solution of triol (**II**) [11] (2.22 g, 6.3 mmol) in pyridine (15 ml) at stirring. The reaction was monitored by TLC, watching the formation of product with R_f 0.4 (10 : 1 chloroform–methanol). After the tritylation was over (16 h), benzoyl chloride (1.74 ml, 15.1 mmol) was added, and the reaction mixture was stirred for 24 h. Then methanol (10 ml) was added at 0°C; the reaction mixture was evaporated; and the residue was dissolved in chloroform (100 ml), washed with 5% aqueous H_2SO_4 (3 × 25 ml), water, and saturated solution of $NaHCO_3$ (3 × 50 ml). The organic layer was dried with Na_2SO_4 and evaporated. The product was isolated by column chromatography on silica gel (40 : 1 toluene—ethyl acetate) to yield 2.30 g (58%) of (**III**); $[\alpha]_D$ +36° (*c* 0.33; $CHCl_3$). ^{1}H NMR: 7.79–7.12 (29 H, m, Ar), 6.25 (1 H, t, $J_{3,2} = J_{3,4}$ = 9.8, H3), 5.75 (1 H, d, $J_{1,2}$ 10.5, H1), 5.70 (1 H, m, H4), 4.75 (1 H, dd, H2), 4.05 (1 H, m, H5), 3.42 (1 H, dd, $J_{6a,5}$ 1.5, $J_{6a,6b}$ 10.5, H6a), 3.30 (1 H, dd, $J_{6b,5}$ 4.9, H6b), 2.85 (1 H, m, SCH_2CH_3), 1.40 (3 H, t, *J* 7.8, SCH_2CH_3); ^{13}C NMR: 168.10, 167.33, 165.85, and 164.88 (four C=O), 143.70 (Tr), 134.33–123.74 (Ar), 86.75 ($C(Ph)_3$); 81.13 (C1), 78.10 (C5), 72.44 (C3), 69.96 (C4), 62.77 (C6), 54.25 (C2), 24.38 (SCH_2CH_3), and 15.50 (SCH_2CH_3).

Ethyl 3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-1-thio-β-*D*-glucopyranoside (IV). Trifluoroacetic acid (10 ml of 90% aqueous solution) was added to a solution of 6-*O*-trityl derivative (**III**) (2.30 g, 2.9 mmol) in CH_2Cl_2 (80 ml). The reaction mixture was stirred for 2 h at room temperature, diluted with $CHCl_3$ (70 ml), and washed with saturated $NaHCO_3$ and water. The organic layer was dried with Na_2SO_4 and evaporated. The residue was chromatographed on silica gel (6 : 1 toluene–ethyl acetate) to yield 1.53 g (95%) of (**IV**); $[\alpha]_D$ +29°; ^{1}H NMR: 7.79–7.12 (14 H, m, Ar), 6.38 (1 H, t, $J_{3,2} = J_{3,4}$ = 9.8, H3), 5.68 (1 H, d, $J_{1,2}$ 10.5, H1), 5.55 (1 H, t, $J_{4,5}$ 9.7, H4), 4.65 (1 H, dd, H2), 3.85 (1 H, m, H5), 3.90 (1 H, d, $J_{6a,6b}$ 11.6, H6a), 3.75 (1 H, dd, $J_{6b,5}$ 3.5, H6b), 2.75 (2 H, m, SCH_2CH_3), 2.60 (1 H, br. s, OH), 1.40 (3 H, t, *J* 7.8, SCH_2CH_3); ^{13}C NMR: 168.14, 167.43, 165.95, and 165.67 (four C=O), 134.31–123.64 (Ar), 81.24 (C1), 78.77 (C5), 71.85 (C3), 70.03 (C4), 61.67 (C6), 54.00 (C2), 24.20 (SCH_2CH_3), and 14.94 (SCH_2CH_3).

3-(9-Fluorenylmethoxycarbonylamino)propanol (Va). *N*-Hydroxysuccinimide (0.68 g, 0.6 mmol) and triethylamine (0.8 ml) were added to a solution of FmocCl (1.20 g, 4.6 mmol) in dioxane (18 ml). The resulting precipitate was filtered off, the filtrate was evaporated, and the residue was dissolved in dioxane. 3-Aminopropanol (0.3 ml, 4 mmol) and triethylamine (0.1 ml) were added; the reaction mixture was stirred for 1 h and evaporated. The residue was subjected to flash chromatography on silica gel (1 : 1 toluene–ethyl acetate) to give 1.10 g (93%) of (**Va**); ^{1}H NMR: 7.78–7.28 (8 H, m, Ar), 5.05 (1 H, br. s, NH), 4.46 [2 H, m, CH_2 (Fmoc)], 4.22 [1 H, m, CH (Fmoc)], 3.65 (2 H, m, $OCH_2CH_2CH_2NH$), 3.31 (2 H, m, $OCH_2CH_2CH_2NH$), 1.68 (2 H, m, $OCH_2CH_2CH_2NH$); ^{13}C NMR: 156.24 (OC(O)NH), 143.90, 141.33, 127.66, 127.02, and 124.94 (Ar), 66.67 (CH_2 (Fmoc)); 59.63 ($OCH_2CH_2CH_2NH$); 47.37 [CH (Fmoc)], 37.79 ($OCH_2CH_2CH_2NH$), 32.60 ($OCH_2CH_2CH_2NH$).

3-Benzyloxycarbonylamino)propanol (Vb). Triethylamine (2 ml) and *N*-(benzyloxycarbonyloxy)succinimide (3.40 g, 13.6 mmol) were added to a solution of 3-aminopropanol (1 g, 13.3 mmol) in a mixture of ethyl acetate (12 ml) and methanol (20 ml). The mixture was stirred for 30 min and evaporated. The residue was dissolved in $CHCl_3$ (60 ml) and washed with 1 M aqueous HCl (3 × 10 ml), water (3 × 10 ml), and $NaHCO_3$ (2 × 10 ml). The extract was filtered though a layer of cotton, evaporated, and crystallized from 1 : 1 ethyl acetate–petroleum ether to yield 2.70 g (95%) of (**Vb**); ^{1}H NMR: 7.40–7.30 (5 H, m, Ar), 5.12 (3 H, br. m, NH and CH_2Ph), 3.67 (2H, m, $OCH_2CH_2CH_2N$); 3.33 (2H, m, $OCH_2CH_2CH_2N$); 2.69 (1 H, br. s, OH), 1.70 (2H, m, $OCH_2CH_2CH_2N$). ^{13}CNMR: 157.30 [OC(O)NH], 136.46, 128.51, 128.12, and 128.07 (Ar), 66.81 (CH_2Ph); 59.59 ($OCH_2CH_2CH_2N$); 37.78 ($OCH_2CH_2CH_2N$); 32.54 ($OCH_2CH_2CH_2N$).

3-(9-Fluorenylmethoxycarbonylamino)propyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside (VI). A mixture of thioglycoside (**I**) (45 mg, 0.1 mmol), 3-Fmoc-aminopropanol (**Va**) (28 mg, 0.1 mmol), freshly distilled dichloromethane (1 ml), and molecular sieve 4Å (100 mg) was stirred for 1 h under argon at room temperature. The resulting mixture was cooled to –20°C, NIS (42 mg, 0.18 mmol) and TfOH (3 μl, 0.04 mmol)were added, the reaction mixture was stirred for 1 h at –15°C, and then pyridine

(10 μl) was added. The resulting suspension was diluted with dichloromethane (20 ml) and filtered though a layer of Celite, which was then washed with dichloromethane (10 ml). The filtrate was washed with 1 M aqueous $Na_2S_2O_3$, dried with Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (10 : 3 toluene–ethyl acetate) to give 57 mg (85%) of (**VI**); ^{1}H NMR: 7.89–7.15 (12 H, m, Ar); 5.78 (1 H, t, $J_{3,2} = J_{3,4} = 9.8$, H3); 5.87 (1 H, d, $J_{1,2}$ 8.8, H1); 5.16 (1 H, t, $J_{4,5}$ 9.6, H4); 4.38–4.20 [3 H, m, H6a, CH_2 (Fmoc)], 4.12 [2 H, m, H6b, CH (Fmoc)], 3.80 (2 H, m, H5, OCH_2CH$_2$CH$_2$NH), 3.53 (1 H, m, OCH_2CH$_2$CH$_2$NH), 3.11 (2 H, m, OCH$_2$CH$_2$CH_2NH), 2.08, 2.04, and 1.87 (9 H, 3 s, CH_3C(O)); 1.68 (2 H, m, OCH$_2$CH_2CH$_2$NH); ^{13}C NMR: 170.66, 170.10, and 169.40 (three C=O), 156.24 [OC(O)NH], 143.86, 141.20 [arom. H (Fmoc)], 134.29–119.85 (Ar), 98.07 (C1), 71.87 (C5), 70.68 (C3), 68.79 (C4), 67.25 (CH_2 (Fmoc)); 66.24 (OCH$_2$CH$_2$CH$_2$NH); 61.74 (C6), 54.47 (C2), 47.21 [CH (Fmoc)], 37.58 (OCH$_2$CH$_2$CH$_2$NH), 29.62 (OCH$_2$CH$_2$CH$_2$NH), 20.68, 20.58, and 20.39 (CH_3C(O)).

1,3,4-Tri-*O*-benzoyl-2-deoxy-2-phthalimido-α- and β-*D*-glucopyranoses (XII) and (XIII). Trityl chloride (11 g, 39.5 mmol) was added to a solution of 2-carboxybenzoyl derivative (**X**) (10 g, 30.5 mmol) in pyridine (100 ml). The reaction mixture was stirred for 24 h at room temperature and diluted with anhydrous dichloromethane (100 ml), and a solution of benzoyl chloride (20 ml, 170 mmol) in dichloromethane (100 ml) was added dropwise. The resulting suspension was stirred for 24 h at room temperature, the excess of benzoyl chloride was quenched with methanol (50 ml), and the reaction mixture was evaporated. The residue was dissolved in chloroform (0.7 l) and washed with 1 M aqueous HCl until the complete removal of pyridine (to acidic pH of the aqueous layer) and saturated aqueous $NaHCO_3$ solution. The organic layer was dried with Na_2SO_4 and evaporated. The residue was dissolved in a mixture of pyridine (60 ml) and acetic anhydride (25 ml). The resulting solution was refluxed for 2 h, poured out onto crushed ice (200 g), and extracted with chloroform (300 ml). The organic layer was washed with 1 M aqueous HCl, water, and saturated aqueous $NaHCO_3$; dried with Na_2SO_4; and evaporated. The resulting residue was dissolved in dichloromethane (100 ml), and 90% aqueous trifluoroacetic acid (1.87 ml) was added. After 1 h, the TFA excess was quenched with saturated aqueous $NaHCO_3$; the organic layer was separated, washed with water, dried with Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (50 : 1–5 : 1) to yield 2.1 g of (**XII**) and 4.7 g of (**XIII**) (total yield 33%).

Compound (**XII**): $[\alpha]_D$ +29°; ^{1}H NMR: 8.38–7.18 (19 H, m, Ar), 6.89 (1 H, d, $J_{1,2}$ 8.9, H1), 6.56 (1 H, t, $J_{3,2} = J_{3,4} = 9.9$, H3), 5.65 (1 H, t, $J_{4,5}$ 9.7, H4), 4.93 (1 H dd, H2), 4.14 (1 H, m, H5), 3.90 (1 H, d, $J_{6a,6b}$ 13.1, H6a), 3.75 (1 H, dd, $J_{6b,5}$ 3.4, H6b); ^{13}C NMR: 166.30, 165.59, and 164.36 (three C=O), 134.39–123.83 (Ar), 90.50 (C1), 75.23 (C5), 70.56 (C3), 69.70 (C4), 60.97 (C6), and 53.86 (C2).

Compound (**XIII**): $[\alpha]_D$ +126°; ^{1}H NMR: 8.38–7.18 (19 H, m, Ar), 7.30 (1 H, m, H3), 6.63 (1 H, d, $J_{1,2}$ 3.7, H1), 5.57 (1 H, t, $J_{4,3} = J_{4,5} = 9.8$, H4), 5.13 (1 H dd, $J_{2,3}$ 11.4, H2), 4.30 (1 H, m, H5), 3.83 (1 H, d, $J_{6a,6b}$ 13.2, H6a), 3.72 (1 H, dd, $J_{6b,5}$ 3.5, H6b); ^{13}C NMR: 166.38, 164.98, and 164.79 (three C=O), 134.29–123.71 (Ar), 91.38 (C1), 75.67 (C5), 70.77 (C4), 67.23 (C3), 60.84 (C6), and 52.99 (C2).

6-*O*-Acetyl-1,3,4-tri-*O*-benzoyl-2-deoxy-2-phthalimido-α-*D*-glucopyranose (XIV). Pyridine (1.5 ml) and acetic anhydride (1 ml) were added to a solution of 6-hydroxy derivative (**XIII**) (2.0 g, 3.2 mmol) in dichloromethane (10 ml). The reaction mixture was stirred for 16 h at room temperature and then evaporated and coevaporated with toluene. The residue was dried at 1 Torr to constant mass to give 2.13 g (100%) of acetate (**XIV**) (100%). $[\alpha]_D$ +89°. ^{1}H NMR: 8.29–7.18 (19 H, m, Ar), 7.25 (1 H, m, H3), 6.62 (1 H, d, $J_{1,2}$ 3.7, H1), 5.70 (1 H, t, $J_{4,3} = J_{4,5} = 10.0$, H4), 5.16 (1 H dd, $J_{2,3}$ 11.5, H2), 4.55 (1 H, m, H5), 4.37 (1 H, d, $J_{6a,5}$ 4.1, $J_{6a,6b}$ 12.4, H6a), 4.21 (1 H, dd, $J_{6b,5}$ 2.7, H6b), 2.06 (3 H, c, CH_3C(O)). ^{13}C NMR: 170.65, 165.37, 164.99, and 164.84 (four C=O), 134.40–123.81 (Ar), 91.27 (C1), 70.32 (C5, C4), 67.53 (C3), 61.96 (C6), 52.91 (C2), 20.76 (CH_3C(O)).

Ethyl 6-*O*-(6-*O*-acetyl-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-1-thio-β-*D*-glucopyranoside (XVI). *Synthesis of bromide* (**XV**). A 33% solution of HBr in AcOH (2 ml) was added to a solution of benzoate (**XIV**) (620 mg, 0.9 mmol) in anhydrous dichloromethane (5 ml). The mixture was stirred for 16 h. The disappearance of starting benzoate (**XIV**) (R_f 0.30) and the formation of bromide (**XV**) as the mixture of α- and β-anomers (R_f 0.35 and 0.40, respectively) were monitored by TLC (20 : 3 toluene–ethyl acetate). The reaction mixture was diluted with dichloromethane (30 ml) and washed with ice-cold water (3 × 5 ml) and saturated aqueous $NaHCO_3$ (3 × 5 ml). The organic layer was filtered through a layer of cotton, concentrated, and dried in a vacuum to give 530 mg (91%) of bromide (**XV**). *Glycosylation.* Mercury (**II**) cyanide (230 mg, 0.9 mmol) and $HgBr_2$ (100 mg, 0.27 mmol) were added to a solution of acceptor (**IV**) (350 mg, 0.62 mmol) in anhydrous acetonitrile (2 ml) under argon. The mixture was stirred for 10 min at room temperature. Bromide (**XV**) was dissolved in anhydrous acetonitrile (5 ml) and added to the solution of the acceptor. The reaction mixture was stirred for 1 h, diluted with chloroform (30 ml), and washed with 1 M aqueous KBr (10 ml) and saturated $NaHCO_3$ (20 ml). The organic extract was filtered through a layer of cotton, concentrated, and dried in a vacuum. The residue was chromatographed on silica gel (15 : 1 toluene–ethyl acetate) to give 580 mg (85%) of disaccharide (**XVI**); ^{1}H NMR: 7.89–7.18 (28 H, m, Ar), 6.22

(2 H, t, $J_{3,2} = J_{3,4}$ = 9.7, H3, H3'), 5.63 (1 H, d, $J_{1,2}$ 8.4, H1'), 5.56–5.53 (2 H, m, H4, H1), 5.38 (1H, t, $J_{4',5}$ 9.6, H4'), 4.58 (1 H, dd, H2'), 4.53 (1 H, t, H2), 4.30 (1 H, d, $J_{6a',5'}$ 5.4, $J_{6a',6b'}$ 5.23, H6a'), 4.21 (1 H, dd, $J_{6b',5'}$ 2.6, H6b'), 4.11–3.95 (3 H, m, H5, H5', H6a), 3.82 (1 H, dd, $J_{6b,5}$ 6.8, $J_{6a,6b}$ 10.9, H6b), 2.55 (2 H, m, SCH_2CH_3), 1.98 (3 H, s, $CH_3C(O)$); 1.13 (3 H, t, J 7.8, SCH_2CH_3); ^{13}C NMR: 170.55, 167.83, 167.07, 165.58, and 165.23 (five C=O), 134.21–123.57 (Ar), 98.17 (C1'), 80.84 (C1), 77.50 (C5), 71.95 (C3', C5'), 71.11 (C3), 70.24 (C4'), 69.93 (C4), 68.57 (C6), 62.51 (C6'), 54.73 (C2'), 53.93 (C2), 24.02 (SCH_2CH_3), 14.92 (SCH_2CH_3), 20.76 ($CH_3C(O)$).

Ethyl 6-*O*-(3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-1-thio-β-*D*-glucopyranoside (XVII). Absolute methanol (10 ml) and acetyl chloride (0.1 ml) were added to a solution of 1-acetate (**XVI**) (520 mg, 0.47 mmol) in dichloromethane (3 ml). The reaction mixture was stirred for 16 h at room temperature, evaporated, and filtered though silica gel (2 : 1 toluene–ethyl acetate) to give 500 mg (100%) of disaccharide (**XVII**); $[\alpha]_D$ +15°; ^1H NMR: 7.95–7.18 (28 H, m, Ar), 6.24–6.20 (2 H, m, H3, H3'), 5.60 (1 H, d, $J_{1',2'}$ 8.5, H1'), 5.53 (1 H, d, $J_{1,2}$ 10.5, H1), 5.46 (1 H, t, $J_{4,3} = J_{4,5}$ = 9.7, H4), 5.33 (1 H, t, $J_{4',3'} = J_{4',5'}$ 9.6, H4'), 4.54 (1 H, t, $J_{2,3}$ 10.4, H2), 4.42 (1 H, dd, $J_{2',3'}$ 10.5, H2'), 4.03–4.15 (2 H, m, H5, H6a), 3.76–3.87 (3 H, m, H5', H6b, H6a'), 3.64 (1 H, dd, $J_{6b',6a'}$ 12.6, H6b'), 2.58 (2 H, m, SCH_2CH_3), 1.13 (3 H, t, J 7.8, SCH_2CH_3); ^{13}C NMR: 165.54 (C=O), 133.97–123.54 (Ar), 97.73 (C1'), 80.93 (C1), 77.00 (C5), 74.40, 71.98, 71.00, 70.83, and 69.95 (C5, C4, C4', C3', C3), 68.47 (C6), 61.32 (C6'), 54.64 and 53.96 (C2, C2'), 23.96 (SCH_2CH_3), 14.93 (SCH_2CH_3).

6-*O*-(3,4-Di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl bromide (XVIII). A solution of Br_2 (0.16 ml) in anhydrous CH_2Cl_2 (1 ml) was added to a solution of thioglycoside (**XVII**) (310 mg, 0.29 mmol). The reaction mixture was stirred for 1 h in the darkness at room temperature. The disappearance of the starting thioglycoside (**XVII**) (R_f 0.25) and the formation of bromide (**XVIII**) (R_f 0.3) was monitored by TLC (4 : 1 toluene–ethyl acetate). The reaction mixture was evaporated and dried in a vacuum to give 315 mg (100%) of bromide (**XVIII**); ^1H NMR: 7.95–7.18 (28 H, m, Ar), 6.38 (1 H, d, $J_{1,2}$ 9.5, H1), 6.30 (1 H, t, $J_{3',2'} = J_{3',4'}$ = 10.4, H3'), 6.14 (1 H, t, $J_{3,2} = J_{3,4}$ = 10.0, H3), 5.65 (1 H, d, $J_{1',2'}$ 8.4, H1'), 5.55 (1 H, t, $J_{4,5}$ 9.8, H4), 5.38 (1 H, t, $J_{4',5'}$ 9.5, H4'), 4.75 (1 H, t H2), 4.48 (1 H, dd, H2'), 4.18–4.04 (2 H, m, H5, H6a), 3.94–3.78 (3 H, m, H5', H6b, H6a'), 3.66 (1 H, dd, $J_{6b',5'}$ 4.5, $J_{6b',6a'}$ 13.0, H6b'); ^{13}C NMR: 165.95, 165.62, and 165.47 (three C=O), 134.65–123.80 (Ar), 98.24 (C1'), 78.04 (C1), 76.60, 74.49 (C5, C5'), 71.04, 70.95, and 69.97 (C3, C4, C3', C4'), 68.52 (C6), 61.26 (C6'), 58.44, and 54.64 (C2, C2').

3-(9-Fluorenylmethoxycarbonylamino)propyl-3,3-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside (XIXa) was obtained by glycosylation as described for disaccharide (**XVI**) from bromide (**XV**) (0.68 mg, 1.1 mmol) and 3-Fmoc-aminopropanol (**Va**) (0.3 g, 1 mmol). Deacetylation analogous to that described for (**XVII**) yielded 740 mg (88%) of spacered ((**XIXa**). $[\alpha]_D$ –2°. ^1H NMR: 7.95–7.18 (22 H, m, Ar), 6.23 (1 H, t, $J_{3,2} = J_{3,4}$ = 9.6, H3), 5.63–5.56 (2 H, m, H1, H4), 5.15 (1 H, br. m, NH), 4.56 (1 H, t, H2), 4.39 [2 H, m, CH_2 (Fmoc)], 4.21 [1 H, m, CH (Fmoc)], 3.91–3.60 (5H, m, H5, H6a, H6b, $OCH_2CH_2CH_2NH_2$); 3.15 (2H, m, $OCH_2CH_2CH_2NH_2$); 1.74 (2H, m, $OCH_2CH_2CH_2NH_2$). ^{13}C NMR: 165.98 and 165.65 (two C=O), 156.42 [OC(O)NH], 143.98 and 141.30 (Fmoc), 134.24–119.94 (Ar), 98.34 (C1), 74.57, 70.98, and 70.11 (C3, C4, C5), 67.29 ($OCH_2CH_2CH_2NH_2$); 66.34 [CH (Fmoc)], 61.33 (C6), 54.83 (C2), 47.37 (CH_2 (Fmoc)], 37.64 ($OCH_2CH_2CH_2NH_2$); 29.51 ($OCH_2CH_2CH_2NH_2$).

3-(Benzyloxycarbonylamino)propyl-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside (XIXb) was obtained analogously to terminator (**XIXa**) from bromide (**XV**) (530 mg, 0.85 mmol) and 3-Z-aminopropanol (**Vb**) (160, mg, 0.77 mmol). Deacetylation resulted in 430 mg (80%) of terminator (**XIXb**); $[\alpha]_D$ +5°; ^1H NMR: 8.78–7.14 (19 H, m, Ar), 6.30 (1 H, t, $J_{3,2} = J_{3,4}$ = 9.9, H3), 5.60 (1 H, d, $J_{1,2}$ 8.5, H1), 5.53 (1 H, t, $J_{4,5}$ 9.6, H4), 5.60 (2 H, br. s, $PhCH_2$), 4.57 (1 H, dd, H2), 3.97–3.63 (5 H, m, H5, H6a, $OCH_2CH_2CH_2NH_2$, H6b), 3.20 (2H, m, $OCH_2CH_2CH_2NH_2$); 1.73 (2H, m, $OCH_2CH_2CH_2NH_2$). ^{13}C NMR: 165.86 and 165.65 (two C=O), 156.37 [O*C*(O)NH], 136.65–123.56 (Ar), 98.34 (C1), 74.71, 71.14, and 70.11 (C3, C4, C5), 67.42 and 66.56 ($OCH_2CH_2CH_2N$, CH_2Ph); 61.38 (C6), 54.88 (C2), 37.83 ($OCH_2CH_2CH_2N$); 29.56 ($OCH_2CH_2CH_2N$).

6-*O*-(6-*O*-Acetyl-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-1,3,4-tri-*O*-benzoyl-2-deoxy-2-phthalimido-α-*D*-glucopyranose (XX) was obtained by the Helferich reaction similarly to disaccharide (**XVI**) from benzoate (**XIV**) (0.95 g) and acceptor (**XIII**) (0.75 g); yield 1.10 g (79%); $[\alpha]_D$ +72°; ^1H NMR: 8.15–7.18 (33 H, m, Ar), 7.09 (1 H, m, H3), 6.34 (1 H, d, $J_{1,2}$ 4.8, H1), 6.22 (1 H, m, $J_{3,2}$ 10.6, $J_{3,4}$ 9.4, H3'), 5.61 (1 H, d, $J_{1',2'}$ 8.4, H1'), 5.60 (1 H, dd, $J_{4',5'}$ 9.7, H4'), 5.45 (1 H, dd, $J_{4,5}$ 9.7, H4), 5.02 (1 H, dd, $J_{2,3}$ 11.5, H2), 4.58 (1 H, dd, H2'), 4.48 (1 H, m, H5), 4.27 (1 H, dd, $J_{6a',5'}$ 5.1, $J_{6a',6b'}$ 12.4, H6a'), 4.22 (1 H, dd, $J_{6b',5'}$ 2.7, H6b'), 4.15 (1 H, dd, $J_{6a,5}$ 1.8, $J_{6a,6b}$ 11.3, H6a), 4.07 (1H, m, H5), 3.77 (1 H, dd, $J_{6b,5}$ 6.1, H6b); 2.05 ($CH_3C(O)$). ^{13}C NMR: 170.60, 167.23, 165.56, 165.14, 165.05, and 164.69 (six C=O), 134.17–123.30 (Ar), 98.63 (C1'), 91.19 (C1), 71.95, 71.47, 71.11, 70.45, 69.81, and 68.27 (C3, C4, C5, C3', C4', C5'), 67.49 (C6), 62.43 (C6'), 54.60, 53.04 (C2, C2'), 20.65 ($CH_3C(O)$).

3-(Benzyloxycarbonylamino)propyl-6-*O*-(3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside (XXII) was obtained as described for terminator (**XIXa**) from benzoate (**XX**) (100 mg, 0.09 mmol) and 3-Z-aminopropanol (**Vb**) (17 mg, 0.08 mmol); yield 80 mg (81%); ^{1}H NMR: 7.95–7.12 (33 H, m, Ar), 6.28 (1 H, t, $J_{3',2'} = J_{3',4'} = 9.4$, H3'), 6.13 (1 H, t, $J_{3,2} = J_{3,4} = 9.9$, H3), 5.60 (1 H, d, $J_{1',2'}$ 8.4, H1'), 5.45 (2 H, m, H4, H1), 5.36 (1 H, t, $J_{4',5'}$ 9.5, H4'), 5.14 (1 H, br. m, NH), 5.04 (2 H, s, CH_2Ph), 4.47 (2 H, m, H2, H2'), 4.05 (2H, m, H5, H6a), 3.88–3.77 (3 H, m, H6b, H5', H6a'), 3.74–3.63 (2 H, m, OCH_2CH$_2$CH$_2$NH$_2$, H6b'), 3.46 (1H, m, OCH_2CH$_2$CH$_2$NH$_2$); 3.05 (2H, m, OCH$_2$CH$_2$CH_2NH$_2$); 1.56 (2H, m, OCH$_2$CH_2CH$_2$NH$_2$). ^{13}C NMR: 167.42, 165.84, 165.05, and 165.59 (four C=O), 134.14–125.27 (Ar), 98.15 (C1), 97.71 (C1'), 74.42 (C5'), 73.15 (C5), 71.17 (C3), 70.85 (C3'), 70.55 (C4), 69.93 (C4'), 67.93 (C6), 67.34 (OCH$_2$CH$_2$CH$_2$NH$_2$); 66.37 (CH_2Ph); 61.21 (C6'), 54.76, 54.57 (C2, C2'), 37.86 (OCH$_2$CH$_2$CH$_2$NH$_2$); 29.36 (OCH$_2$CH$_2$CH$_2$NH$_2$).

Ethyl 6-*O*-[6-*O*-(3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl]-3,4-di-*O*-benzoyl-2-deoxy-2-phthalimido-1-thio-β-*D*-glucopyranoside (XXIII) was synthesized as described for disaccharide (**XVI**) from benzoate (**XX**) (250 mg, 0.22 mmol) and acceptor (**IV**) (115 mg, 0.2 mmol); yield 246 mg (75%); ^{1}H NMR: 7.95–7.05 (42 H, m, Ar), 6.24 (1 H, t, $J_{3'',2''} = J_3$, H3''), 6.18 (1 H, t, $J_{3,2} = J_{3,4} = 9.8$, H3), 6.11 (1 H, t, $J_{3',2'} = J_{3',4'} = 9.5$, H3'), 5.58 (1 H, d, $J_{1'',2''}$ 8.4, H1''), 5.54 (1 H, d, $J_{1,2}$ 10.5, H1), 5.49 (1 H, d, $J_{1',2'}$ 8.4, H1'), 5.37 (2 H, m, H4, H4'), 5.29 (1 H, t, $J_{4'',5''}$ 9.6, H4''), 4.54 (1 H, t, H2), 4.41 (1 H, dd, H2'), 4.34 (1 H, dd, H2''), 4.05 (1 H, dd, $J_{6a',5'}$ 4.1, $J_{6a',6b'}$ 10.7, H6a'); 4.01–3.94 (3 H, m, H6a, H5, H5'), 3.90 (1 H, m, H5''), 3.85–3.79 (2 H, m, H6a'', H6b'), 3.71 (1 H, dd, $J_{6b'',5''}$ 5.2, $J_{6b'',6a''}$ 12.5, H6b''), 2.60 (2 H, m, SCH_2CH$_3$), 1.15 *J* 8, SCH$_2$CH_3). ^{13}C NMR: 167.09, 165.56, and 165.13 (three C=O), 134.05–123.50 (Ar), 97.86 and 97.42 (C1', C1''), 80.83 (C1), 74.24, 72.60, 71.99, 71.06, 70.83, 70.33, and 69.82 (C3–C5, C3'–C5', C3''–C5''), 68.21, and 67.88 (C6, C6'), 61.27 (C6''), 54.68, 54.60, and 53.87 (C2, C2, C2''), 23.92 (S*C*H$_2$CH$_3$), 14.96 (SCH$_2$*C*H$_3$).

Terminated oligomerization (IV) + (Va). A mixture of monomer (**IV**) (430 mg, 0.77 mmol), 3-Fmoc-aminopropanol (**Va**) (45 mg, 0.15 mmol), freshly distilled dichloromethane (10 ml), and molecular sieves 4 Å (1 g) was stirred for 1 h under argon at room temperature. The resulting mixture was cooled to –20°C, NIS (345 mg, 1.53 mmol) and TfOH (27 μl, 0.3 mmol) were added, and the reaction mixture was stirred for 1 h under argon at –15°C. According to TLC (3 : 2 toluene–ethyl acetate), the starting monomer (R_f 0.55) disappeared, and the reaction mixture contained the products with R_f 0.7 (the main product) and R_f 0.6. Pyridine (50 μl) was added to the reaction mixture; the resulting suspension was diluted with dichloromethane (20 ml) and filtered through a layer of Celite, which was then washed with dichloromethane (40 ml). The filtrate was washed with 1 M aqueous $Na_2S_2O_3$, dried with Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (9 : 1 toluene–ethyl acetate) to give 220 mg (50%) of anhydro derivative (**VII**) and 85 mg (20%) of cyclic disaccharide (**VIII**).

Compound (**VII**): MS, *m/z* 521.9 $[M + Na]^+$ (calculated for $C_{28}H_{21}NO_8$ *M* 499.13); $[\alpha]_D$ –5°; ^{1}H NMR: 8.18–7.22 (14 H, m, Ar), 6.22 (1 H, t, $J_{3,2}$ 9.2, H3), 5.80 (1 H, s, H1), 5.22 (1 H, d, $J_{4,3}$ 8.1, H4), 4.85 (1 H, d, $J_{5,6b}$ 5.3, H5), 4.55 (1 H, d, H2), 4.30 (1 H, d, $J_{6a,6b}$ 7.8, H6a), 4.00 (1 H, dd,H6b); ^{13}C NMR: 167.58, 166.48, and 165.93 (three C=O), 134.36–123.71 (Ar), 102.35 (C1), 78.02 (C4), 76.92 (C5), 68.86 (C3), 68.26 (C6), 56.07 (C2).

Compound (**VIII**): MS, *m/z* 1021.1 $[M + Na]^+$ (calculated for $C_{56}H_{42}N_2O_{16}$ *M* 998.26); $[\alpha]_D$ –39°; ^{1}H NMR: 7.94–7.18 (14 H, m, Ar), 6.40 (1 H, t, $J_{3,2} = J_{3,4} = 10.5$, H3), 6.05 (1 H, dd, $J_{4,5}$ 6.5, H4), 5.50 (1 H, d, $J_{1,2}$ 4.2, H1), 5.03 (1 H, dd, H2), 4.42 (1 H, d, $J_{5,4}$ 6.5, H5), 4.05 (1 H, d, $J_{6a,6b}$ 10.4, H6a), 3.98 (1 H, d, H6b); ^{13}C NMR: 167.47, 165.71, 165.34 (three C=O), 134.06–123.68 (Ar), 98.47 (C1), 78.37 (C5), 70.54 (C4), 68.77(C3), 66.08 (C6), 55.13 (C2).

Oligomerization(III) + (Va). A mixture of monomer (**III**) (100 mg, 0.12 mmol), terminator (**Va**) (8 mg, 0.025 mmol), freshly distilled dichloromethane (1 ml), and molecular sieves 4 Å (200 mg) was stirred for 1 h under argon at room temperature. Methyl triflate (82 μl, 0.75 mmol) was then added. After 1 h, TLC (5 : 1 toluene–ethyl acetate) showed the absence of the starting monomer (R_f 0.70) and prevalence of the product (R_f 0.65. The reaction mixture was evaporated and chromatographed on silica gel (50 : 1 – 10 : 1 toluene–ethyl acetate) to give 50 mg (55%) of glycal (**IX**), 13 mg (15%) of (**VII**), and 8 mg (10%) of (**VIII**).

Compound (**IX**): $[\alpha]_D$ –70°; ^{1}H NMR: 8.08–7.15 (29 H, m, Ar), 6.90 (1 H, s, H1), 5.88 (1 H, d, $J_{3,4}$ 3.3, H3), 5.77 (1 H, t, $J_{4,5}$ 4.0, H4), 4.57 (1 H, m, H5), 3.90 (1 H, dd, $J_{6a,5}$ 7.4, $J_{6a,6b}$ 10.9, H6a), 3.58 (1 H, dd, $J_{6b,5}$ 4.0, H6b); ^{13}C NMR: 167.66, 165.67, and 164.83 (three C=O), 143.62 (Tr), 134.15–123.63 (Ar, C2), 105.00 (C1), 87.31 (C(Ph)$_3$), 76.34 (C5), 67.67 (C4), 66.70 (C3), 61.59 (C6).

Terminated oligomerization (XVII) or (XVIII) + (Va) (a series of experiments). Experiment no. 1. The reaction was carried out as described for (**IV**) + (**Va**) using monomer (**XVII**) (30 mg, 30 μmol), terminator (**Va**) (2 mg, 6 μmol), freshly distilled dichloromethane (250 μl), NIS (13 mg), and TfOH (2 μl) in the presence of molecular sieves 4 Å at –15°C. The disappearance of the starting monomer (R_f 0.35) and the generation of almost the only product (visualization with H_3PO_4) with R_f 0.45, which was identified on the basis of NMR spectrum as the cyclic disaccharide (**VIII**), were monitored by TLC (2 : 1 toluene–ethyl acetate).

Experiment no. 2. The reaction was carried out as described for (**IV**) + (**Va**) using monomer (**XVII**) (50 mg, 47 μmol), terminator (**Va**) (3 mg, 9 μmol), freshly distilled dichloromethane (125 μl), NIS (13 mg), and TfOH (2 μl) in the presence of molecular sieves 4 Å at –40°C. According to TLC, the results were identical to those obtained in the Experiment no. 1.

Experiment no. 3. (**XVIII**) + (**Va**) terminated oligomerization.

Experiment no. 4. The reaction was carried out as described for (**IV**) + (**Va**) using monomer (**XVIII**) (30 mg, 28 μmol), terminator (**Va**) (2 mg, 6 μmol), freshly distilled dichloromethane (175 μl), and AgOTf (15 mg) in the presence of molecular sieves 4 Å at –15°C. According to TLC of the reaction mixture, the results were identical to those obtained in Experiment no. 1.

Experiment no. 5. The reaction was carried out as described in Experiment no. 1 using freshly distilled acetonitrile (250 μl) as a solvent in the presence of molecular sieves 3Å. According to TLC of the reaction mixture, the results were identical to those obtained in Experiment no. 1.

Terminated oligomerization (XVIII) + (Va). Mercury(II) cyanide (100 mg, 0.4 mmol) and $HgBr_2$ (40 mg, 0.11 mmol) were added to a solution of terminator (**Va**) (18 mg, 0.06 mmol) in anhydrous CH_3CN (0.3 ml) under argon; the mixture was stirred for 10 min at room temperature; a solution of bromide (**XVIII**) in anhydrous CH_3CN (0.5 ml) was added to the solution of the acceptor; and the reaction mixture was stirred for additional 1 h. According to TLC (2 : 1 toluene–ethyl acetate), the reaction mixture contained no starting bromide (**XVIII**) (R_f 0.50) and exhibited a separate spot with R_f 0.55 and a lane of spots from the start line to R_f 0.40. The product with R_f 0.55 was isolated by chromatography on silica gel to give 87 mg (30%) of cyclic disaccharide (**VIII**).

Analysis of the oligomerization results (Method 1). *Removal of Fmoc group*. The mixture of oligomers (240 mg) obtained after the (**XVIII**) + (**Va**) terminated oligomerization and separation of the cyclic product was dissolved in anhydrous THF (1 ml), ethanethiol (0.07 ml, 0.9 mmol) and DBU (3 μl, 0.02 mmol) were added, and the mixture was stirred for 20 min. Thin layer chromatography in 5 : 1 $CHCl_3$–MeOH demonstrated the appearance of ninhydrin-positive spots with R_f 0.1–0.3. Acetic acid (20 μl) was added, the reaction mixture was evaporated, the residue was dissolved in 1 : 4 CH_2Cl_2–MeOH, and Amberlyst 15 (Fluka) ion-exchange resin (H^+) was added up to complete sorption of ninhydrin-positive compounds (TLC monitoring). The suspension of cation exchanger was transferred to a chromatographic column and washed with 1 : 4 CH_2Cl_2–MeOH. The terminated products were eluted with a mixture of MeOH (100 ml), CH_2Cl_2 (25 ml), and concentrate HCl (5 ml). The resulting mixture of terminated oligomers was dissolved in ethanol (5 ml); hydrazine hydrate (0.5 ml) was added, and the reaction mixture was refluxed for 1 h. Then the reaction mixture was evaporated and dried in a vacuum. The residue was chromatographed on TSK HW-40(S) (25–40 μm) gel column (80 × 2.5 cm) in 0.1 M AcOH to give 12 mg (10%) of disaccharide (**XXVII**, n = 1); ^{1}H NMR: 4.75 and 4.77 (2 H, 2 d, H1, H1'), 4.31 (1 H, t, $J_{6a, 6b}$ 10.1, H6a), 4.10 (1 H, m, $OCH_2CH_2CH_2NH_2$), 4.04–3.97 (2 H, m, H6b, H6a'), 3.88 (1 H, m, $OCH_2CH_2CH_2NH_2$), 3.84 (1 H, dd, $J_{6b', 5'}$ = $J_{6b', 6a'}$ = 12.4, H6b'), 3.75 (1 H, m, H5), 3.68 (2 H, m, H3, H3'), 3.63 (1 H, m, $J_{4, 3}$ 9.3, H4), 3.59–3.52 (2 H, m, H5', H4'), 3.21 (2 H, m, CH $OCH_2CH_2CH_2NH_2$), 3.09–3.01 (2 H, m, H2, H2'), 2.08 (2 H, m, $OCH_2CH_2CH_2NH_2$); ^{13}C NMR: 101.25 (C1, C1'), 77.34 (C5'), 75.78 (C5), 73.98 and 73.89 (C3, C3'), 70.82 (C4'), 70.59 (C4), 69.50 (C6), 68.94 ($OCH_2CH_2CH_2NH_2$), 61.54 (C6'), 56.95 (C2, C2'), 38.41 ($OCH_2CH_2CH_2NH_2$), 27.95 ($OCH_2CH_2CH_2NH_2$).

Oligomerization(XVIII) + (XIXa). The reaction was carried out similarly to (**XVIII**) + (**Va**) oligomerization using bromide (**XVIII**) (70 mg) and terminator (**XIXa**) (11 mg). According to TLC, the result of the reaction was analogous to that of the (**XVIII**) + (**Va**) oligomerization.

Analysis of the results of oligomerization (Method 2). The products obtained by oligomerization (**XVIII**) + (**XIXa**) were analyzed as follows: gel chromatography on BioBeads SX-3 (BioRad) in toluene of the reaction mixture helped isolate the monosaccharide fraction consisting of the unreacted terminator (5 mg), the disaccharide fraction containing cyclic disaccharide (**VIII**) and the product of monomer hydrolysis (**XVII**), and an oligomeric fraction, which was then analyzed as described in Method 1. Trisaccharide (**XXVII**, n = 2) was obtained; yield 4 mg (12%); MS, m/z: 559.2 [M + H]$^+$ (calculated for $C_{21}H_{42}N_4O_{13}$ M 558.3).

Oligomerization (XVIII) + (XIXa) with graduate addition of monomer. Bromide (**XVIII**) (100 mg, 0.1 mmol in 300 μl of anhydrous acetonitrile) was added in 60 μl portions at 30-min intervals to a solution of terminator (**XIXa**) (15 mg, 0.02 mmol), $Hg(CN)_2$, (24 mg, 0.1 mmol), and $HgBr_2$ (10 mg, 0.03 mmol) in anhydrous acetonitrile (50 μl) at stirring under argon. The reaction mixture was treated as described for the (**XVIII**) + (**Va**) oligomerization. The reaction products were analyzed by Method 2. Yield: 4 mg of terminator (**XIXa**), 7 mg (15%) of terminated trisaccharide (**XXVII**, n = 2), and traces of pentasaccharide (**XXVII**, n = 4); MS, m/z: 881.3 [M + H]$^+$ (calculated for $C_{33}H_{64}N_6O_{21}$ M 880.4).

Terminated oligomerization (XVIII) + (XIXb). The reaction was carried out and analyzed using monomer (**XVIII**) (100 mg, 0.1 mmol) and terminator (**XIXb**) (14 mg, 0.02 mmol) as described for the (**XVIII**) + (**XIXa**) oligomerization. *Removal of the Fmoc group.* The mixture obtained after oligomerization was dissolved in 20 : 30 : 0.8 : 0.5 *i*-PrOH–THF–

AcOH–H_2O mixture, a catalytic amount of 10% Pd/C was added, and the mixture was stirred for 16 h under hydrogen at room temperature. The reaction mixture was filtered through a layer of Celite; the filtrate was evaporated; and then the reaction products were analyzed by Method 2. Yield: 5.5 mg (12%) of terminated trisaccharide (**XXVII**, $n = 2$) and traces of pentasaccharide (**XXVII**, $n = 4$).

Terminated oligomerization (XVIII) + (XXII). The reaction was carried out using monomer (**XVII**) (50 mg, 0.05 mmol) and terminator (**XXII**) (9 mg, 0.007 mmol) as described for the (**XVII**) + (**XVIII**) oligomerization. The reaction products were analyzed by Method 2. Yield: 12 mg (25%) of cyclic disaccharide (**VIII**) and 7 mg (14%) of terminated oligomers (**XXVII**).

Terminated oligomerization (XXIII) + (XXII). The reaction was carried out using trisaccharide monomer (**XXIII**) (30 mg, 0.02 mmol) and terminator (**XXII**) (5 mg, 4 μmol) as described for (**XVII**) + (**Va**) oligomerization; yield 27 mg (95%) of cyclic trisaccharide (**XXVIII**). $[\alpha]_D$ +44°. ^{1}H NMR: 7.90–7.18 (42 H, m, Ar), 6.15 (1 H, t, $J_{3,2} = J_{3,4} = 10.2$, H3), 5.77 (1 H, d, $J_{1,2}$ 8.2 H1), 5.56 (1 H, t, $J_{4,5}$ 9.52, H4), 4.68 (1 H, dd, H2), 4.19 (1 H, dd, $J_{6a,5}$ 5.4, $J_{6a,6b}$ 12.6, H6a), 4.14 (1 H, m, H5), 3.90 (1 H, dd, H6b); ^{13}C NMR: 165.80 and 164.74 (two C=O), 133.94–123.55 (Ar), 97.28 (C1), 73.78 (C5), 71.37 (C3), 69.75 (C4), 68.41 (C6), 55.02 (C2).

Terminated oligomerization (XXIV) + (XXII). The reaction was carried out using trisaccharide (**XXIV**) (75 mg, 46 μmol) and terminator (**XXII**) (10 mg, 8 μmol) as described for oligomerization (**XVIII**) + (**XIXa**); yield 36 mg (50%) of cyclic trisaccharide (**XXVIII**)

ACKNOWLEDGMENTS

This work was supported by CRDF grant no. RUB1-2639-MO-05 and Russian Foundation for Basic Research, project no. 05-03-08107.

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