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Synthetic Conversion of Cellobiose into the Glycal-Type Monomers and Their Polymerization

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Abstract

A pair of disaccharidic glycals thoroughly *O*-benzylated except the 4'- or the 6'-hydroxyl groups were prepared as the monomers for iodonium ion-promoted polymerization, which proceeded under dark conditions to give polysaccharides of more than DP 12 (24 saccharide). Reductive removal of the iodine atom and subsequent deprotection gave polysaccharides alternatively composed of β-D-glucopyranosyl and 2-deoxy-α, β-D-glucopyranosyl residues.

Keywords: Dealkylation; Glycals; Glycosidation; Polymerization

In spite of recent advances in the *O*-glycosidation methodology for oligosaccharide syntheses, successful polymerization of saccharidic monomers has been very limitted to a few examples such as ring-opening polymerizations of 1,6-anhydro sugars [1], orthoesters [2], and cyanoethylidene derivatives [3]. Different from these successful examples, condensation polymerizations of monomers possessing anomeric leaving groups like an alkylmercapto group [4] seem to have met difficulties for elongation of the polymer chain. Besides, the degree of polymerization (DP_n) further decreased when a disaccharidic monomer was used [5]. As another type of glycosidation methodology, there is an oxidatively triggered addition of alcohols to glycals via 1,2-iodonium ion formation [6]. This stereoselective haloetherification of glycals has been successfully applied to a variety of oligosaccharide syntheses [7] but not to polymerization processes yet.

Here we describe an application of that haloetherification to a pair of disaccharidic glycal monomers for their polymerization. The monomers were derived from cellobiose, overcoming unexpected deprotection problems encountered at the glycal formation. Polymerization of these monomers assisted by iodonium addition revealed that light influenced the reaction process in an inhibitory manner. Consequently, satisfactory results were obtained by the polymerization conducted under protection from the light.

Cellobiose is readily obtainable by degradation of cellulose and reconstruction of novel polymers from it is of great mean as a production of potential new materials. We expected

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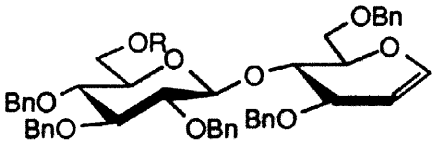
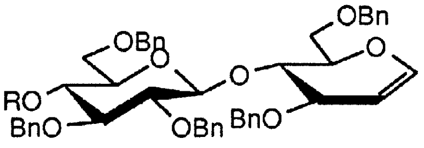
the preparation of 1,5-anhydro-3,6-di-*O*-benzyl-2-deoxy-4-*O*-(2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl)-D-*arabino*-hex-1-enitol (**1a**) and 1,5-anhydro-3,6-di-*O*-benzyl-4-*O*-(2,3,6-tri-*O*-benzyl-β-D-glucopyranosyl)-D-*arabino*-hex-1-enitol (**2a**) as the disaccharidic monomers, starting from the known cellobiose derivative, phenyl 2,2',3,3',6-penta-*O*-benzyl-4',6'-*O*-benzylidene-1-thio-β-cellobioside (**3**) [8].

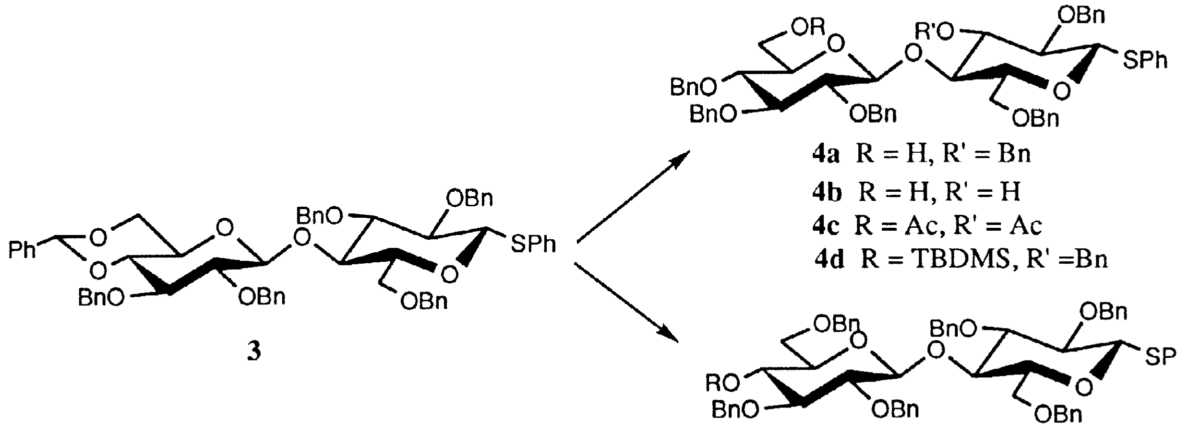


1a R = H
1b R = TBDMS



2a R = H
2b R = TBDMS

Reductive cleavage of the benzylidene group of **3** with $BH_3\cdot Me_3N\text{-}AlCl_3$ proceeded regioselectively, depending on the solvents employed [9]. Thus, the reaction in CH_2Cl_2 [10] gave the 4'-benzyloxy-6'-hydroxy compound **4a**, mp 152 °C, $[\alpha]_D^{26}$ +7.5°[1], as the major product, whereas 6'-benzyloxy-4'-hydroxy compound **5a**, mp 113 °C, $[\alpha]_D^{26}$ -11°, was obtainable by the reaction in tetrahydrofuran (THF). Sinay et al. [11] reported that treatment of thioglycosides in THF at low temperature with lithium naphthalenide caused reductive lithiation at C-1 followed by elimination of the 2-substituent to give the glycal derivatives in excellent yields. When this reaction was applied to **4a**, the substrate unexpectedly underwent selective debenzylation at the 3-position without any change of its thioglycoside group, giving in 35% yield the 3,6'-dihydroxyl compound **4b**, mp 150 °C, $[\alpha]_D^{28}$ -2.4°, accompanied with **4a** recovered in 38% yield. The structure of **4b** was elucidated by NMR analyses of its acetylated derivative **4c**, ^{1}H NMR[2] δ 5.19 (dd, 1H, $J_{2,3}$ = 9.3 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 1.94 and 1.84 (each s, 3H, OAc). In the case of **5a**, a similar treatment with lithium naphthalenide



3

4a R = H, R' = Bn
4b R = H, R' = H
4c R = Ac, R' = Ac
4d R = TBDMS, R' =Bn

5a R = H
5b R = TBDMS

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[1] All compounds with the specific rotation data gave the satisfactory results of elemental analyses. The solvent for the specific rotation measurements was $CHCl_3$ in all cases.

[2] Unless otherwise specified, $CDCl_3$ was used as the solvent for NMR measurements.

gave a mixture of several products without recovery of **5a**. Although the expected glycal **2a** was isolated from the mixture in 32% yield, most of other products were supposed to be partially deprotected compounds. These results suggested that the free hydroxyl groups located in the nonreducing monosaccharide moieties might interfere with the action of lithium naphthalenide for conversion of the thioglycoside moiety into the glycal. Therefore, the free hydroxyl groups of **4a** and **5a** were to be protected before the glycal formation. Thus, each of **4a** and **5a** were treated with *t*-butyldimethylsilyl chloride in the presence of imidazole in *N,N*-dimethylformamide (DMF), giving quantitatively the 6'-*O*-silylated derivative **4d** and the 4'-*O*-silylated one **5b** in syrupy forms: **4d**, $[\alpha]_D^{23}$ -5.8°; **5b**, $[\alpha]_D^{29}$ +2.6°. In contrast to **4a** and **5a**, **4d** and **5b** underwent smooth conversion into the coressponding glycals, **1b** (99%) and **2b** (92%) on treatment with lithium naphthalenide in THF: **1b**, $[\alpha]_D^{21}$ -3.8°, ^{1}H NMR δ 6.48 (d, 1H, $J_{1,2}$ = 6.3 Hz, H-1), 4.90 (m, 1H, H-5), 4.19 (br s, 1H, H-4), 4.05 (br s, 1H, H-3); **2b**, $[\alpha]_D^{28}$ +11.6°, ^{1}H NMR δ 6.52 (d, 1H, $J_{1,2}$ = 6.3 Hz, H-1), 4.35 (br s, 1H, H-5), 4.29 (br s, 1H, H-4), 4.21 (br s, 1H, H-3). For removal of the silyl protecting group at C-6 or C-4 positions, **1b** and **2b** were treated with tetra *n*-butylammonium fluoride in THF, giving crystalline **1a** and syrupy **2a** almost quantitatively: **1a**, mp 93 °C, $[\alpha]_D^{28}$ +15.2°, ^{1}H NMR δ 6.44 (d, 1H, $J_{1,2}$ = 6.2 Hz, H-1); **2a**, $[\alpha]_D^{29}$ -13.8°, ^{1}H NMR δ 6.52 (d, 1H, $J_{1,2}$ = 6.6 Hz, H-1).

Polymerization of the prepared disaccharidic monomers was conducted in CH_2Cl_2 at room temperature under argon atmosphere by treatment with I(*sym*-collidine)$_2$ClO$_4$ (3 mol. eq.) and stopped by addition of 2-propanol to the viscous mixture resulted after 3 days. The mixture was analyzed by gel permeation chromatography (GPC) using Shodex KF802.5 column. The GPC pattern of **6a** obtained by preliminary polymerization of **1a** is shown in Fig.1, which discloses the production of a polymer mixture containing the component of DP_n 4 as the longest detectable one. However, subsequent experimental repetitions showed the

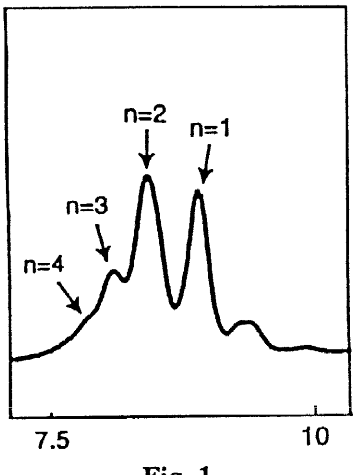


Fig. 1

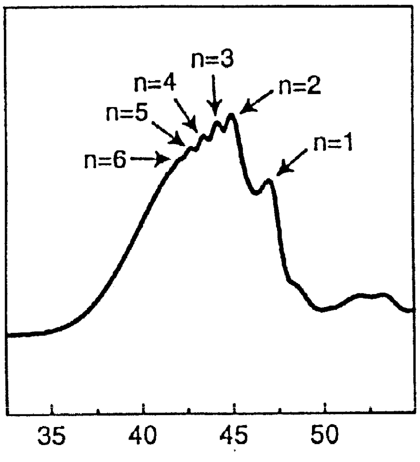


Fig. 2

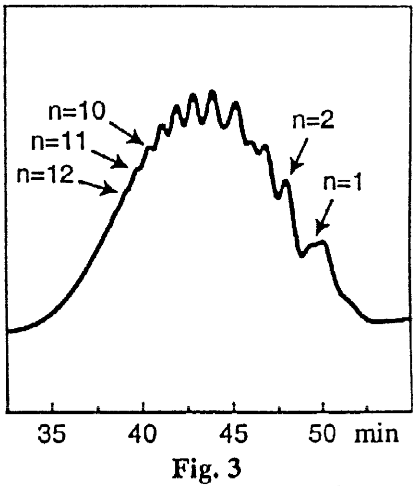
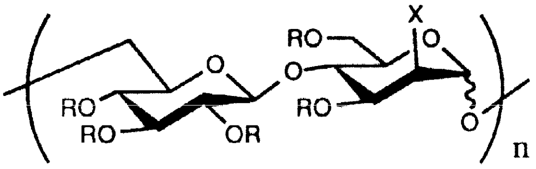


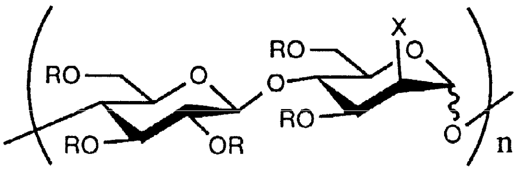
Fig. 3

All GPC was performed by using THF as the mobile phase with the flow rate 0.3-1.0 ml/min and a UV detector.

lack of reproducibility of this polymerization reaction. This problem was completely removed when the reaction was carried out in a sealed *brown* flask. Besides, such a reaction brought about a remarkable increase of DPn. Fig. 2 shows the GPC pattern of **6a** obtained from **1a** under the reaction conditions shielded from light, which reveals the production of polymers with DP_n more than 6. On the basis of these experimental results, **2a** was also polymerized under dark conditions in the same way as **1a**, giving a polymer mixture **7a** as shown in Fig.3. Apparently, polymer chains longer than 24 saccharides (DP_n 12) were produced by the polymerization of **2a**.



6a R = Bn, X = I
6b R = Bn, X = H
6c R = H, X = H



7a R = Bn, X = I
7b R = Bn, X = H
7c R = H, X = H

Each of polymer mixtures **6a** and **7a**[3] were then treated in toluene at 50→80 °C with tributyltin hydride in the presence of AIBN, giving deiodinated polymers, **6b** and **7b**, both of which showed negative Beilstein test. It was confirmed by comparing GPC patterns between the substrates and the products that neither **6a** nor **7a** underwent chain cleavages during that radical reduction. Finally, **6b** and **7b** were thoroughly debenzylated by repeated catalytic hydrogenations in the presence of $Pd(OH)_2$ / C, with the solvent systems changed (DMF-acetic acid→DMF-water-acetic acid→water-acetic acid). In ^{13}C-NMR spectra (D_2O) of the obtained polymers, α anomeric carbons appeared as sole signal (**6c**, δ 98.41; **7c** δ 98.39), whereas β anomeric carbons as a pair of signals (**6c**, δ 102.73 and 102.60; **7c**, δ 102.71 and 102.59), suggesting that this polymerization was devoid of stereoselectivity in difference from the exclusive α–glycosidation in low molecular oligosaccharide syntheses.

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[3] In CMR specrum ($CDCl_3$) of this compound, signals due to the anomeric carbons could not be definitely assigned, because most of those anomeric carbons resonated with the different chemical shifts in such a fully protected carbohydtrate polymer as 7_a.