Notes

Regioselectively Modified Stereoregular Polysaccharides. 11. Synthesis of (1→6)-α-D-Glucopyranans Having One Long Hydrocarbon Chain in Position 3 in Each Repeating Unit

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Introduction

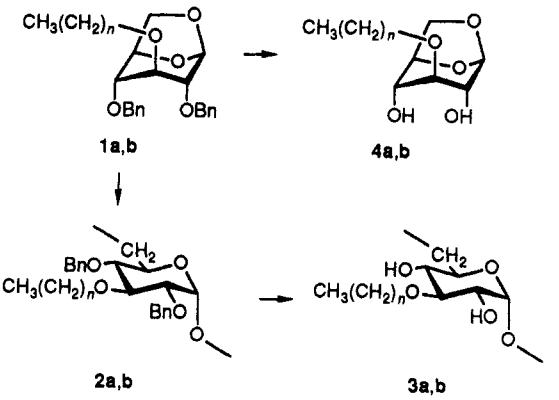
Mono-, oligo-, and polysaccharides having long hydrocarbon chains are widely distributed in nature. Glycolipids play an important role in specific recognition of cells,[1] lipid A is a potent substance of endotoxin,[2] and microbial exocellular polysaccharides (emulsan) have become significant industrial products in recent years.[3] Analogous simple alkylated substances obtained synthetically have a prospect of developing the new field of application as specialty materials, namely as carbohydrate liquid crystals,[4-6] detergents for solubilization of membrane proteins,[7] synthetic biomembranes,[8-12] highly ordered helical superstructures,[13,14] and polysaccharide-coated liposomes.[15,16]

In this paper, we have synthesized structurally well-defined amphiphilic polysaccharides, that is, 3-*O*-octadecyl- and 3-*O*-dodecyl-(1→6)-α-D-glucopyranans (**3a** and **3b**, respectively) as shown in Scheme I. Each repeating glucopyranose unit of polysaccharide **3** carries two hydroxyl groups at C-2 and C-4 and one long alkyloxy group at C-3. In other words, a regular array of hydrophobic long alkyl chains protrudes from a hydrophilic polysaccharide main chain. Such well-defined polysaccharides consisting of the amphiphilic structural unit cannot be prepared by direct chemical modifications of polysaccharides. The polysaccharide synthesis via stereospecific ring-opening polymerization is useful for this purpose.[17-19]

We previously reported[20-23] that homopolymerizations of 1,6-anhydro-2,4-di-*O*-benzyl-3-*O*-octadecyl-β-D-glucopyranose (**1a**) and the dodecyl homologue (**1b**) proceeded promptly in the presence of phosphorus pentafluoride as initiator in dichloromethane at −60 °C to give (1→6)-α-linked polymers (**2a,b**) with high molecular weight. However, conventional debenzylation of the homopolymers **2** using sodium in liquid ammonia was unsuccessful, although the debenzylation of copolymers between **1** and 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose proceeded successfully to give partially octadecylated and dodecylated polysaccharides.[21-23] We assumed that the failure of debenzylation of the homopolymers **2** was attributed to poor compatibility of both of the reactants and products with the inorganic reagents.

In the present work, we have employed another debenzylation method, radical bromination–hydrolysis.[24,25] We applied the method first to the monomeric anhydro compounds **1** and then to the polymerisates **2**. It has been shown that the method is effective when the product is soluble in organic solvents. We expect that the debenzylation method will extend the scope of polysaccharide synthesis via ring-opening polymerization.

Scheme I
Synthesis of 3-*O*-Octadecyl- (3a) and 3-*O*-Dodecyl-(1→6)-α-D-glucopyranans (3b) and 1,6-Anhydro-3-*O*-octadecyl- (4a) and 1,6-Anhydro-3-*O*-dodecyl-β-D-glucopyranoses (4b)



Experimental Section

Characterization. ^1H and ^{13}C NMR spectra were obtained with a JEOL JNM-FX 200 Fourier transform NMR spectrometer operating at 200 and 50 MHz, respectively. Optical rotations were determined in a Japan Spectroscopic Co. DIP-181 digital polarimeter using a water-jacketed 1-dm cell. Gel permeation chromatography (GPC) was carried out on a Hitachi 634A high-performance liquid chromatograph with a Shodex GPCA 803-804 (8 mm i.d. × 1000 mm) column. Chloroform and polystyrene were used as solvent and standard, respectively. Number-average molecular weights of debenzylated polymers were determined with a Hewlett-Packard vapor pressure osmometer on solutions in benzene at 37 °C. Viscosities were determined in a Ubbelohde viscometer at 25 °C.

1,6-Anhydro-3-*O*-Octadecyl-β-D-glucopyranose (4a). 1,6-Anhydro-2,4-di-*O*-benzyl-3-*O*-octadecyl-β-D-glucopyranose (**1a**)[22] (0.20 g, 0.34 mmol) was dissolved in 20 mL of chloroform in an open beaker, powdered sodium carbonate was added, and the mixture was cooled to 0 °C in an ice bath. Bromine (0.68 mmol) solution in chloroform was added, and the stirred mixture was irradiated from above with a 60-W incandescent bulb. Immediately, **1a** (R_f 0.80), benzaldehyde (R_f 0.74), and two intermediates (R_f 0.66 and 0.60) were detected on TLC (1/1 (v/v) hexane–ethyl acetate). Two 0.51-mmol portions of bromine were added after 1.5 and 3.5 h, and the reaction was continued at 0 °C (total irradiation time 4.5 h). TLC showed the conversion of **1a** and two intermediates to **4a** (R_f 0.24). Water (30 mL) was added, sodium carbonate in the beaker was dissolved, and the mixture was stirred at room temperature for 6 h. The chloroform layer was separated, dried over sodium sulfate, and concentrated. The residue was purified by silica gel column chromatography to give a white powder: yield 0.073 g (53%); $[\alpha]^{25}_D$ −27.7° (*c* 1.0 in chloroform); ^{13}C NMR ($CDCl_3$) δ 101.5 (C-1), 80.1 (C-3), 76.1 (C-5), 70.6 (octadecyl CH_2O), 69.0 (C-2), 67.9 (C-4), 64.7 (C-6),

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Table I
Synthesis of 3-O-Octadecyl- and 3-O-Dodecyl-(1→6)-α-D-glucopyranan (3a and 3b)

exptl no.	starting polymer		product					
	polymer	$\bar{M}_n$[a] × 10^{-4}	polymer	yield, %	$[\alpha]^{25}_D$,[b] deg	$\bar{M}_n$[a] × 10^{-4}	$\bar{M}_n$[c] × 10^{-4}	$[\eta]$,[d] dL/g
4[e]	**2a**	38	**3a**	86	+82.4	3.0		0.14
3[f]	**2a**	38	**3a**	43[h]	+78.4	0.82	0.30	0.06
2[e]	**2b**	23	**3b**	59	+108.6	2.2		0.10
1[g]	**2b**	10	**3b**	63[i]	+108.0	1.7	1.4	0.09

[a] Determined by GPC (polystyrene standard). [b] c = 1 g/100 mL in chloroform. [c] Determined by vapor pressure osmometry in benzene at 37 °C. [d] In chloroform at 25 °C. [e] Bromination–hydrolysis was carried out three times in the presence of powdered molecular sieves 4A (3.0 equimolar bromine was used in total). [f] Bromination–hydrolysis was repeated twice (1.4 equimolar bromine was used in total). [g] Bromination–hydrolysis was repeated twice (2.5 equimolar bromine was used in total). [h] Anal. Calcd for $(C_{24}H_{46}O_5)_n$: C, 69.52; H, 11.18. Found: C, 69.71; H, 11.01. [i] Anal. Calcd for $(C_{18}H_{34}O_5)_n$: C, 65.42; H, 10.37. Found: C, 65.43; H, 9.92.

31.9, 29.9, 29.7, 29.4, 29.3, 26.1, and 22.7 (octadecyl CH_2), 14.1 (CH_3). Anal. Calcd for $C_{24}H_{46}O_5$: C, 69.52; H, 11.18. Found: C, 69.49; H, 11.25.

1,6-Anhydro-3-O-dodecyl-β-D-glucopyranose (4b): yield 61%; $[\alpha]^{25}_D$ −34.5° (c 1.0 in chloroform); mp 54–57 °C. Anal. Calcd for $C_{18}H_{34}O_5$: C, 65.42; H, 10.37. Found: C, 65.50; H, 10.31.

2,4-Di-O-benzyl-3-O-octadecyl- (2a) and 2,4-Di-O-benzyl-3-O-dodecyl-(1→6)-α-D-glucopyranan (2b). Cationic ring-opening polymerization of **1a** and **1b** was carried out with phosphorus pentafluoride as an initiator in dichloromethane at −60 °C.[21,22]

2a: $[\alpha]^{25}_D$ +83.1° (c 1.0 in chloroform); $[\eta]$ = 0.85 dL/g (in chloroform at 25 °C); $\bar{M}_n = 2.3 \times 10^5$ (membrane osmometry in toluene solution at 37 °C). **2b**: $[\alpha]^{25}_D$ +98.5°; $[\eta]$ = 1.29 dL/g; $\bar{M}_n = 4.3 \times 10^5$.

Debenzylation of Polymers 3. A representative experiment was as follows. Polymer **2a** (0.29 g) was dissolved in 15 mL of chloroform in a 100-mL beaker, and 1.5 g of powdered sodium carbonate and 2.0 g of powdered molecular sieves 4A were added. The mixture was cooled to 0 °C in an ice bath. Bromine (0.16 g, an equivalent amount of the benzyl group of **2a**) was added, and the mixture was irradiated with a 60-W incandescent bulb at 0 °C for 1 h. Saturated sodium carbonate solution (10 mL) was added, and the mixture was stirred vigorously at room temperature for 2 h and filtered through Celite. The chloroform layer was separated, dried over sodium sulfate, and concentrated in vacuo. The product was reprecipitated from its chloroform solution into methanol three times and freeze-dried from its benzene solution. The ^{1}H NMR spectrum of the polymer (recovery, 0.24 g) showed that ca. 70% of the benzyl group was removed during the first treatment. The second debenzylation of the recovered polymer was carried out in the same manner and ca. 80% of the benzyl group was removed (recovery, 0.23 g). The third debenzylation gave a perfectly debenzylated polymer **3a** as a white powder: yield 0.18 g (86%); ^{13}C NMR of **3b** ($CDCl_3$) δ 98.1 (C-1), 82.8 (C-3), 73.1 (C-2), 72.6 (C-5), 69.9 (C-4 and octadecyl CH_2O), 66.7 (C-6), 31.9, 30.5, 29.7, 29.4, 26.1, and 22.7 (octadecyl CH_2), 14.1 (CH_3).

Results and Discussion

Debenzylation via Radical Bromination–Hydrolysis. Debenzylation of 1,6-anhydro-2,4-di-O-benzyl-3-O-octadecyl-β-D-glucopyranose (**1a**) in chloroform was performed in the presence of bromine and sodium carbonate under irradiation with an incandescent bulb at 0 °C. Monitoring by thin-layer chromatography indicated that benzaldehyde and two intermediates (probably monobenzyl isomers) were detected immediately, although consumption of **1a** was slow. Finally, compound **1a** and the two intermediates were converted into one product, 1,6-anhydro-3-O-octadecyl-β-D-glucopyranose (**4a**). Removal of the octadecyl chain was not observed under the conditions used.

According to the mechanism proposed by BeMiller et al.,[24,25] the reaction involves (1) free-radical bromination of one of the methylene hydrogen atoms of benzyl ether ($ROCH_2C_6H_5$) in organic solution and (2) mild alkaline hydrolysis of the resulting α-bromobenzyl ether ($ROCHBrC_6H_5$) in aqueous solution via α-hydroxybenzyl ether ($ROCH(OH)C_6H_5$) to yield a hydroxyl component (ROH) and benzaldehyde. The present debenzylation of **1a** was attained by a one-step operation in chloroform solution since both the reactants and products were soluble in the solvent. It was supported experimentally that radical bromination was the rate-determining step, and the α-bromobenzyl and α-hydroxybenzyl components were unstable and promptly hydrolyzed.

Debenzylation of stereoregular polysaccharide derivatives **2a** and **2b** is summarized in Table I. An equimolar amount of bromine was used in order to avoid main-chain scission which was brought about by generated hydrogen bromide. The reaction was repeated until no benzyl signals were detectable in the ^{1}H NMR spectrum of the isolated product. In exptl nos. 1 and 3, complete debenzylation was attained by the two repeated procedures, but chain scission still occurred and some of the products were lost during the workup procedure. In exptl nos. 2 and 4, powdered molecular sieves 4A were added as a scavenger for hydrogen bromide. Consequently, polymer **3a** with a molecular weight of 3×10^4 ($\overline{DP}_n$ = 72) was obtained in 86% yield.

Complete debenzylation was confirmed by the elemental analytical data described in the footnotes of Table I and by the ^{13}C NMR spectrum in the Experimental Section. No β-anomeric signal was detected, and optical rotations were positive and large, suggesting the α-stereoregularity of the polymers. White powdery polysaccharides **3a** and **3b** were soluble in dichloromethane, chloroform, benzene, tetrahydrofuran, and pyridine and insoluble in hexane, acetone, ethyl acetate, methanol, dimethyl sulfoxide, and water.

Solution Properties of Polysaccharide 3 in Chloroform. When a chloroform solution containing **3a** (25 mg in 20 mL) was shaken with an aqueous methyl orange solution (5.0×10^{-4} mol/L, 10 mL), the chloroform layer was colored and an absorption of methyl orange (λ_{max} = 421 nm; absorbance 0.18) was observed in the visible spectrum of the chloroform solution. Since methyl orange is insoluble in chloroform and an aqueous methyl orange solution is not miscible with chloroform, the methyl orange solution is solubilized into chloroform with the help of the amphiphilic polysaccharide. The solubilizing ability of **3b** was weaker than that of **3a**, while **4a** showed no detectable solubilizing ability.

^{13}C NMR signals of the sugar moiety of **3b** were broader than those of the hydrocarbon moiety, and those of **3a** were too broad to be detected.

A reasonable interpretation of these findings is as follows. Mobility of the hydrophilic polysaccharide backbone of **3**, especially of **3a**, was reduced in chloroform, and hydrophilic microdomains were formed through clustering of the polysaccharide moieties.

Investigation of side-chain crystallization and thermotropic behavior is now on progress.

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Communications to the Editor

Time Dependence of the Storage Modulus of Polycarbonate following Temperature Jumps within the Glassy State

Introduction. It has long been known that the physical properties of an amorphous polymer in the glassy state depend on its thermal and mechanical histories. An early detailed study was made by Kovacs,[1,2] who quenched specimens from the equilibrium rubbery state to the glassy state and then monitored the slow but continuous decrease in volume under isothermal conditions. (The volume never reaches a constant value in any ordinary experimental time, except when the temperature is no more than 15 or possibly 20 °C below T_g.) The decrease in volume is accompanied by a progressive reduction in the mobility of short molecular segments that produces a continuous increase in the retardation times. Consequently, following a quench from above T_g, the viscoelastic and other physical properties become time dependent under isothermal conditions, as shown by a number of studies.[2-5] Struik[4,5] has termed such phenomena physical aging, a term selected because the aging can be reversed by heating a specimen above T_g or it can be partially, if not completely, reversed by subjecting the specimen to a mechanical deformation.[4,6]

At part of his studies, Kovacs observed a phenomenon commonly termed a memory effect.[2,7] Specifically, after volume recovery (volume decrease) has occurred for a significant period at temperature T_1 that is substantially below T_g, the temperature is increased stepwise to T^*, which is still below T_g. At T^*, the volume first increases for a period (after temperature equilibrium has been established), then it passes through a maximum, and finally it decreases, eventually joining the original volume–time curve. Similar behavior has also been found during the intermittent measurement of creep curves, each for a relatively short period.[4,8] First, such curves were determined during physical aging at a relatively low temperature, reached by quenching the specimen from above T_g. Then, after a temperature jump to a higher temperature, which is still below T_g, the creep compliance, from the repeated measurements of short-term creep curves, was found to increase for a period, then to pass through a maximum, and finally to decrease continuously. These manifestations of the memory effect show that at least two, but in reality a broad distribution of, retardation times exist.

The present investigation of a well-annealed polycarbonate film was made to determine how its storage modulus in tension, E', depends on the elapsed time after a specimen has been subjected to two types of temperature jumps. For each jump, the initial and final temperatures are below T_g. Most previous studies of changes of mechanical properties during physical aging have been made on specimens that had been quenched from above to below T_g.

Experimental Section. A film of Bisphenol A polycarbonate 0.13-mm thick (Lexan from the General Electric Co.) was annealed for 1 h at 160 °C, then cooled slowly to 120 °C and annealed for 1 mo at this temperature, and finally cooled slowly to room temperature. This material was used in a study[9] at temperatures from −110 to +110 °C of the rate of physical aging of specimens maintained at a static elongation of 2.6%.

In the present study, a specimen was mounted in the tensile unit of a DMTA (dynamic mechanical thermal analyzer produced by Polymer Laboratories, Inc.) at room temperature, which is about 20 °C. The temperature was then increased at 20 °C/min to one of a series of temperatures above 20 °C. Each specimen was next subjected

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