Novel Polysaccharide Surfactants: Synthesis of Model Compounds and Dextran-Based Surfactants

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ABSTRACT: Two novel dextran surfactants, *N*-*n*-hexyldextran aldonamide (diblock AB type) and *N*,*N*′-hexamethylenebis(dextran aldonamide) (triblock ABA type), which were composed of hydrophilic dextran oligosaccharide ($M_w = 1600$) and hydrophobic hexamethylene, were synthesized and characterized by GPC, FTIR, and ^{1}H-NMR. The dextran surfactants were prepared by the selective oxidation and lactonization of the reducing end groups of dextran oligosaccharide, followed by the aminolysis with hexylamine or 1,6-hexanediamine. The intermediate lactones reacted selectively with amines to form the amide linkages, obviating the need for protecting the hydroxyl groups in the dextran. To optimize the reaction conditions and purification methods, model compounds were synthesized from D-maltose monohydrate. An ion-exchange chromatography method was developed to purify the dextran surfactants, based on the fact that the dextran surfactants are nonionic while the impurities are ionic. In addition to linear diblock and triblock polysaccharide surfactants with different block chain lengths, the synthetic approach described in this report also provides a practicable route for the preparation of starlike and comblike polysaccharide surfactants.

Introduction

Considerable effort has been devoted to the surface modification of synthetic polymers used for biomedical cardiovascular applications in order to reduce the clinical problem of surface-induced thrombosis.[1,2] This has included attachment by covalent or ionic chemical bonding of molecules with anticoagulant properties such as heparin[3] and synthetic polymers that exhibit protein-resistant properties such as poly(ethylene oxide).[4] While some improvement in blood compatibility has been achieved, the chemical immobilization techniques lack the ability to control the surface molecular architecture, surface density, and critical properties of the selected immobilized molecules.

Recently, we began exploring the constructive use of hydrophobic interaction and effect to create a new biomaterial interface capable of minimizing "nonspecific" protein adsorption. For this purpose, a novel polysaccharide surfactant composed of hydrophilic dextran and hydrophobic hexamethylene was developed in our laboratory and used to modify the surface of polyethylene in aqueous solution.[5] The adhesion between the physisorbed polysaccharide surfactant and polyethylene was shown to be stable even under conditions of high shear, and the modified polyethylene showed significant resistance to protein adsorption.[5] A similar approach also has been reported using poly(ethylene oxide)/poly(propylene oxide) (PEO/PPO) block copolymer surfactants physisorbed on polyethylene and polystyrene.[6,7] However, the hydrophobicity of the PPO segment was considered insufficient to maintain adequate adhesion stability under applied shear.

These initial studies have shown that physical adsorption offers advantages over chemical bonding in that surface modification can be realized in a simple single step and controlled in a quantitative manner. However, there are several factors that need to be addressed in order to draw quantitative conclusions that might lead to an optimized molecular design for the surfactant. Computer simulation studies indicate that chain length, conformational flexibility, surface chain density, and substrate topography affect the adsorption and the strength of the repulsion barrier in aqueous media.[8] The polysaccharide surfactant used in our previous research was synthesized by the reaction of dextran with epichlorohydrin under neutral conditions, followed by the coupling reaction with 1,6-hexanediamine.[5] Since the reaction of epichlorohydrin with the hydroxyl groups in dextran is not selective toward the reducing end, the linkage to the hydrophobic segment could be anywhere along the dextran chain. The initial objective of this research was to develop a synthetic method to prepare polysaccharide surfactants with well-defined molecular structures in order to improve our understanding of the adsorption behavior and surface properties. We chose dextran as the hydrophilic block for the surfactants, because the α(1→6) linkage between the D-glucose repeating units of dextran affords high chain flexibility.[9] Dextran has been modified selectively by reductive amination[10] and selective oxidation[11] by targeting the lone aldehyde group located at the reducing end of the molecule, but, to our knowledge, the synthesis of dextran-based triblock polysaccharide surfactant has not been reported previously. In this report, we describe the synthesis of linear, dextran-based di- and triblock polysaccharide surfactants and model compounds prepared by oxidation, lactonization, and aminolysis reactions.

Experimental Section

(1) Materials. D-Maltose (4-*O*-α-D-glucopyranosyl-D-glucose) monohydrate (Sigma Chemical Co.), dextran ($M_w = 1600$, $M_w/M_n = 1.16$) (Fluka Chemical Co.), iodine, and silver carbonate (Aldrich Chemical Co.) were used as received. Hexylamine, 1,6-hexanediamine, and dimethyl sulfoxide (DMSO) were purchased from Aldrich Chemical Co. and freshly distilled before use. Strong cationic exchange resin, Amberlite *IR-120 (sulfonic acid functional group)*, was purchased from Aldrich Chemical Co. and rinsed with distilled water before use. Weak cationic exchange resin, Amberlite IRC-50 (carboxylic acid functional group), and weak anionic

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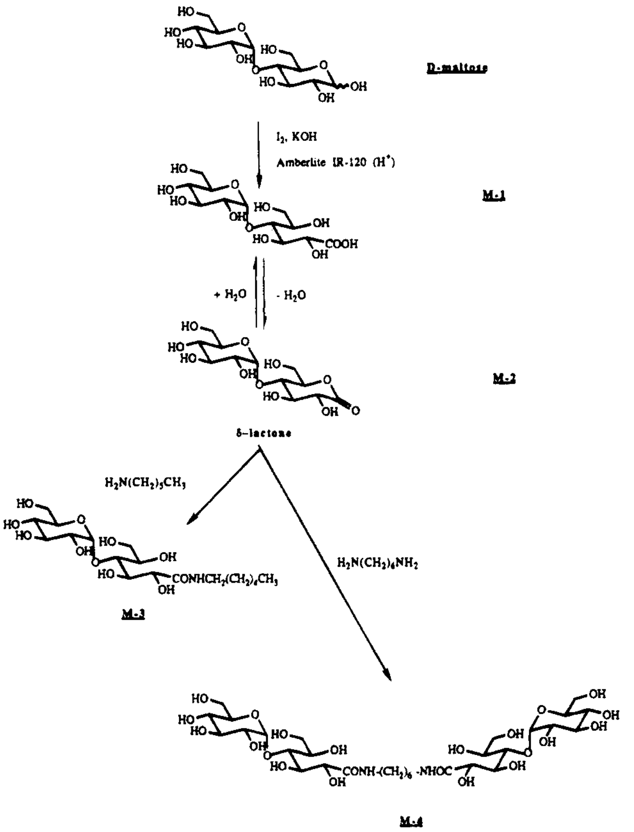
Scheme 1. Model Compounds from D-Maltose



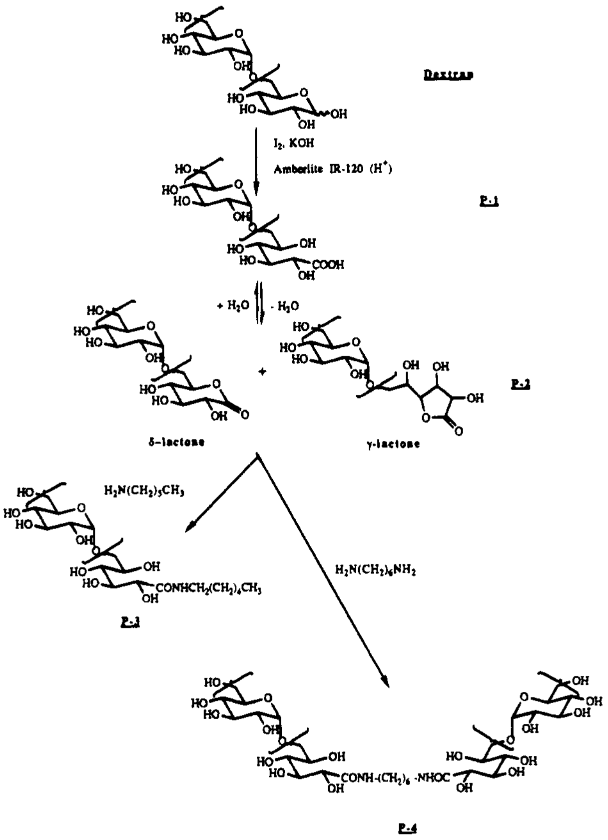
exchange resin, Amberlite IRA-94 (primary amine functional group), were purchased from Sigma Chemical Co. and rinsed with distilled water before use. The desalination media, Sephadex G15 (particle size 40-120 μm), was purchased from Pharmacia Biotech Inc. and rinsed with distilled water before use. All other reagents and solvents were used as received unless otherwise specified.

(2) Methods. ^{1}H-NMR spectra were recorded at ambient temperature, using a 200 MHz Varian XL-200 spectrometer, in parts per million downfield from tetramethylsilane (TMS) as internal standard and DMSO-d_6 as solvent. Transmission IR spectra in the range 400–4000 cm^{-1} were recorded using a Digilab FTS-40 FTIR spectrometer. Solutions were cast on KBr disks and dried under vacuum before measurements. Powdered materials were ground with KBr powder and pressed into pellets under reduced pressure. For each sample, 256 scans were collected with a resolution of 8 cm^{-1}. Gel permeation chromatography (GPC) measurements were carried out using a HEMA-BIO100 GPC column equipped with a Rainin HPXL solvent delivery system and a DYNAMAX refractive index detector. The column was calibrated with dextrans with narrow molecular weight distribution. The flow rate was 1.0 mL/min with distilled water as eluent.

(3) Synthesis of Model Compounds from D-Maltose. The synthetic route and designations for the model compounds are shown in Scheme 1.

D-Maltonolactone (M-2). To a 20 mL aqueous solution containing 1.8 g (5 mmol) of D-maltose monohydrate were slowly added 2.54 g (10 mmol) of iodine in 100 mL of water and 2.24 g (40 mmol) of potassium hydroxide in 30 mL of water. The reaction mixture was stirred at ambient temperature for 2 h and passed through a strong cationic exchange column (2.5 cm i.d. × 40 cm *L*) packed with Amberlite IR-120. The eluate was treated with 5.5 g (20 mmol) of silver carbonate to precipitate excess iodine as silver iodide. The eluate was filtered, and the filtrate again was passed through the Amberlite IR-120 column (regenerated using 200 mL of 1 M HCl solution) to convert silver maltonate to D-maltonic acid (M-1). GPC analysis indicated that 98% of the D-maltose was oxidized to M-1. The M-1 solution was concentrated and lyophilized to give 1.53 g (90% yield) of D-maltonolactone (M-2). IR (KBr): 1740 cm^{-1} (ν(C=O) in δ-lactone).

Scheme 2. Dextran Surfactants



***N-n*-Hexyl-D-maltonamide (M-3).** To a 10 mL DMSO solution containing 0.68 g (2.0 mmol) of M-2 was added 2.02 g (20 mmol) of hexylamine. The reaction solution was stirred at 60 °C for 2 days and then concentrated to 2 mL by vacuum distillation. The product was precipitated in chloroform. The precipitate was washed with ethyl ether and dried under vacuum at 60 °C overnight to give a white powder. The powder was dissolved in 40 mL of distilled water and passed through a weak anionic exchange column (2.5 cm i.d. × 50 cm *L*) packed with Amberlite IRA-94. The eluate was concentrated and lyophilized to give 0.5 g (57% yield) of M-3. IR (KBr): 1650 (amide I), 1544 cm^{-1} (amide II). ^{1}H-NMR (DMSO-d_6, ppm): δ 0.86 (3H, CH$_3$), 1.25–1.40 (8H, CH$_3$(CH_2)$_4$), 3.03–4.00 (14H, CONHCH_2 and all maltose CH's and CH$_2$'s except the one at the glycosidic linkage), 4.46–5.52 (9H, CH at the glycosidic linkage and all OH's), 7.56 (1H, CONH).

***N,N'*-Hexamethylenebis(D-maltonamide) (M-4).** To a 10 mL DMSO solution containing 0.68 g (2 mmol) of M-2 was added 58 mg (0.5 mmol) of 1,6-hexanediamine. The mixture was stirred at 60 °C for 3 days and then concentrated to 2 mL by vacuum distillation. The product was precipitated in chloroform. The precipitate was filtered and dried under vacuum at 60 °C overnight to give a slightly yellow powder. The product was dissolved in 40 mL of water and passed through a weak anionic exchange column (2.5 cm i.d. × 50 cm *L*) packed with Amberlite IRA-94 and a weak cationic exchange column (2.5 cm i.d. × 50 cm *L*) packed with Amberlite IRC-50. The eluate was concentrated and lyophilized to give 0.22 g (55% yield) of M-4. IR: 1650 (amide I), 1544 cm^{-1} (amide II). ^{1}H-NMR (DMSO-d_6, ppm): δ 1.20–1.40 (8H, (CH$_2$)$_4$), 3.09–4.00 (28H, CONHCH_2 and all maltose CH's and CH$_2$'s except the one at the glycosidic linkage), 4.48–5.56 (18H, CH at the glycosidic linkage and all OH's), 7.58 (2H, CONH).

(4) Synthesis of Dextran Surfactants. The synthetic route and designations for the dextran surfactants are shown in Scheme 2.

Dextran Lactone (P-2). To a 10 mL aqueous solution containing 2.76 g (2 mmol) of dextran (M_w = 1600, M_w/M_n = 1.16) were slowly added 1.01 g (4 mmol) of iodine in 40 mL of water and 0.90 g (16 mmol) of potassium hydroxide in 20 mL of water. The reaction mixture was stirred at ambient temperature for 24 h and desalted by passing through a Sephadex G15 column (3.0 cm i.d. × 50 cm *L*). The dextran fractions were passed through a strong cationic exchange column (2.5 cm i.d. × 40 cm *L*) packed with Amberlite IR-120 to convert dextran potassium aldonate to dextran aldonic acid (P-1). GPC indicated that about 96% of the dextran was oxidized. The eluate was concentrated and lyophilized to give 2.40 g (87% yield) of dextran lactone (P-2). IR (KBr): 1771 (ν(C=O) in γ-lactone), 1745 cm^{-1} (ν(C=O) in δ-lactone).

***N*-*n*-Hexyldextran Aldonamide (P-3).** To a 4 mL DMSO solution containing 0.55 g (0.4 mmol) of P-2 was added 2.02 g (20 mmol) of hexylamine. The reaction solution was stirred at 60 °C for 4 days, and the product was precipitated in chloroform. The precipitate was filtered and dried under vacuum at 60 °C overnight to give a white powder. The powder was dissolved in 50 mL of water and passed through a weak anionic exchange column (2.5 cm i.d. × 50 cm *L*) packed with Amberlite IRA-94. The eluate was concentrated and lyophilized to give 0.30 g (50% yield) of P-3. IR (KBr): 1646 (amide I), 1547 cm^{-1} (amide II). ^{1}H-NMR (DMSO-d_6, ppm): δ 0.87 (CH_3), 1.25–1.40 ($CH_3(CH_2)_4$), 3.00–4.04 ($CONHCH_2$ and all dextran CH's and CH_2's except the ones at the glycosidic linkages), 4.39–5.32 (CH's at the glycosidic linkages and all OH's), 7.82 (CONH).

***N*,*N'*-Hexamethylenebis(dextran aldonamide) (P-4).** To a 4 mL DMSO solution containing 0.55 g (0.4 mmol) of P-2 was added 11.6 mg (0.1 mmol) of 1,6-hexanediamine. The solution was stirred at 60 °C for 6 days, and the product was precipitated in chloroform. The precipitate was filtered and dried under vacuum at 60 °C overnight to give a yellow powder. The powder was dissolved in 40 mL of water and passed through a weak anionic exchange column (2.5 cm i.d. × 50 cm *L*) packed with Amberlite IRA-94 and a weak cationic exchange column (2.5 cm i.d. × 50 cm *L*) packed with Amberlite IRC-50. The eluate was concentrated and lyophilized to give 0.10 g (34% yield) of P-4. IR: 1646 (amide I), 1547 cm^{-1} (amide II). ^{1}H-NMR (DMSO-d_6, ppm): δ 1.20–1.40 ($(CH_2)_4$), 3.00–4.04 ($CONHCH_2$ and all dextran CH's and CH_2's except the ones at the glycosidic linkages), 4.39–5.32 (CH's at the glycosidic linkages and all OH's), 7.82 (CONH).

Results and Discussion

Model Compounds from D-Maltose. Our goal was to develop synthetic and purification methods based on model compound studies that could be specifically adopted for the synthesis of dextran polysaccharide surfactants. For this purpose, D-maltose was chosen as the model compound for dextran, because it has the same D-glucose repeating unit. The oxidation, lactonization, and aminolysis of D-maltose have been reported previously.[11-13] However, in our experiments, we paid particular attention to the solubility differences between maltose and dextran, so that we used solvents for the model compounds that were also solvents for the polysaccharides. Accordingly, we used water rather than methanol as the solvent for the oxidation of maltose, because dextran is soluble in water but insoluble in methanol. As the solubility properties of reactant and final product are similar, the polysaccharide surfactants could not be purified by recrystallization or precipitation. We circumvented this problem by developing of an ion-exchange chromatography method of purification, based on the functional group difference between the reactant and final product.

Following the procedure of Hashimoto et al.,[11] we used an aqueous solution of I_2/KOH to oxidize the reducing end group of D-maltose. The GPC traces of D-maltose and the oxidation product after passage through a strong cationic exchange column are shown in Figure 1. It was found that 98% of D-maltose was oxidized to maltonic acid (M-1) after 2 h of reaction. Interestingly, we observed that M-1 showed a shorter GPC column retention time than D-maltose, even though their molecular weights are similar. We think that the GPC column is somewhat negatively charged, so that elution of M-1 is accelerated by electrostatic repulsion. According to the supplier, the column packing material, cross-linked hydroxyethyl methacrylate (HEMA), is treated to reduce residual hydrophobicity, and this procedure may introduce negatively charged groups. The hypothesis is consistent with our observations that hexylamine and 1,6-hexanediamine are retained on the column, while the retention time of M-1 increases with increasing concentration, eventually merging with the elution of D-maltose to form a broad single peak. Thus, positively charged amines are retained on the column because of electrostatic attraction with the negatively charged matrix, while the retention time of M-1 increases with increasing concentration, because the density of negatively charged groups on the matrix is relatively low. Ziegast and Pfannemuller reported similar observations when analyzing the oxidation products of amylose oligosaccharides on Bio-Gel columns.[14] The packing media for the Bio-Gel columns consist of cross-linked polyacrylamides, which are thought to hydrolyze under weak acidic or basic conditions to produce carboxylate.[14]

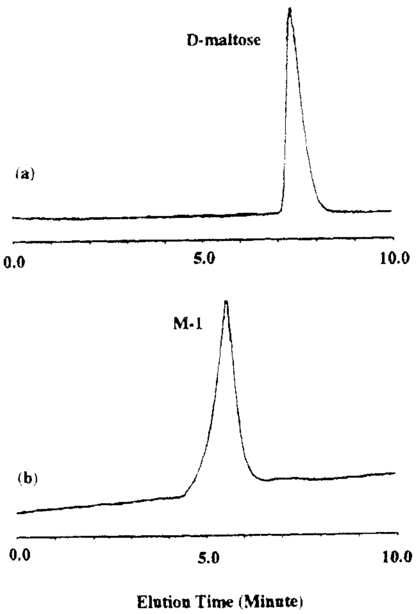


Figure 1. GPC traces of (a) D-maltose and (b) the oxidation product of D-maltose after 2 h of reaction. GPC was carried out on a HEMA-BIO100 column at a flow rate of 1.0 mL/min using water as eluent.

D-Maltonic acid (M-1) was converted quantitatively to D-maltonolactone (M-2) by lyophilization. The hydroxyl group at the δ position of M-1 cyclized with the carboxylic acid to form δ-lactone (1,5-lactone, six-membered ring) with the liberation of water. The carbonyl stretching peak of δ-lactone at 1740 cm^{-1} is shown clearly in the IR spectrum of M-2 (Figure 2). The peak attributable to carbonyl stretching of the free acid, which should be around 1700 cm^{-1}, is not observed. There is some water associated with M-2, as indicated by the presence of a weak δ(O–H) peak at 1643 cm^{-1}, a peak which is also present in the IR spectrum of D-maltose monohydrate. It should be noted that M-2 is sensitive to the presence of water and will hydrolyze back to M-1. Thus, in the GPC trace of M-2 (retention time = 7.4 min) eluted with water, a peak attributable to M-1 was observed. M-2 should be kept dry at all the

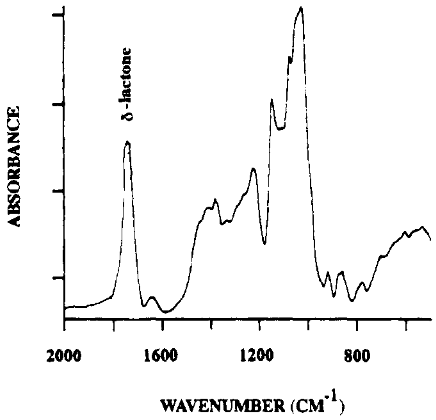


Figure 2. Transmission IR spectrum (2000–500 cm^{-1} region) of D-maltonolactone (M-2).

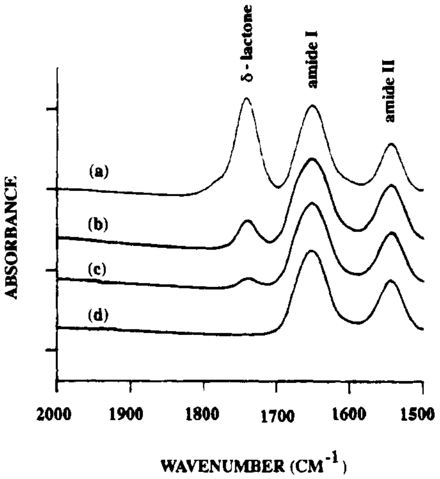


Figure 3. Transmission IR spectra (2000–1500 cm^{-1} region) of the reaction product of D-maltonolactone with hexylamine after reaction at 60 °C for (a) 2, (b) 6, (c) 24, and (d) 48 h.

times. Similarly, solvents and reagents used in the aminolysis reaction require vigorous drying.

N-*n*-Hexyl-D-maltonamide (M-3) was synthesized by the reaction of maltonolactone (M-2) with hexylamine. To achieve high conversion from lactone to amide, excess hexylamine (1/10 molar ratio of lactone to amine) was used. The reaction of M-2 with hexylamine at 60 °C may be followed by FTIR, since the lactone and amide have characteristic peaks. As shown in Figure 3, we observed that the carbonyl stretching peak, ν(C=O) in lactone at 1740 cm^{-1} decreased, while the ν(C=O) at 1650 cm^{-1} and the δ(N–H) at 1544 cm^{-1}, corresponding to the amide I and amide II absorptions of M-3, increased with reaction time. M-2 was consumed completely after 48 h, as indicated by the disappearance of the peak at 1740 cm^{-1}.

N,*N'*-Hexamethylenebis(D-maltonamide) (M-4) was synthesized by the reaction of maltonolactone (M-2) with 1,6-hexanediamine. Since both ends of 1,6-hexanediamine have to be reacted to form M-4, the key to high M-4 yield is high amine to amide conversion. For this purpose, excess M-2 (1/2 molar ratio of amine to lactone) was used. Although the IR spectrum showed the formation of amide, it did not provide an indicator for completion of the reaction, which depended on the consumption of amine. Instead of using FTIR to follow the carbonyl groups, we used ^{1}H-NMR because the chemical shift of protons on the carbon atom adjacent to the amine changed from 2.75 (CH_2NH_2) to 3.09 ppm (CH_2NHCO) after reaction. As expected, the peak at 2.75 ppm decreased, while the peak at 3.09 ppm increased with reaction time. While the peak at 3.09 ppm overlaps with the maltose multiplets, we were able to the follow the reaction by monitoring the disappearance of the 2.75 ppm peak. After 3 days at 60 °C, the peak at 2.75 ppm was no longer detectable, indicating that most amines were converted to amides.

Both M-3 and M-4 were purified by ion-exchange chromatography. In the case of M-3, the precipitated product was almost pure M-3, because excess hexylamine dissolved in chloroform. The possible impurity was a trace amount of M-2, which was removed by hydrolyzing to M-1 and passing through a weak anionic exchange column (Amberlite IRA-94, primary amine functional group). M-1 was retained on the column because of electrostatic attraction between the carboxylic acid of M-1 and the amine of matrix. In the case of M-4, the precipitated product included M-4, excess M-2, and some monoamidated product. As before, M-2 was hydrolyzed to M-1 and removed by passing through a weak anionic exchange column. The amine-terminated, monoamidated product was removed by passing through a weak cationic exchange column (Amberlite IRC-50, carboxylic acid functional group). After ion-exchange purification, the purity of M-3 and M-4 was over 98% as indicated by GPC. The retention times of D-maltose, M-2, M-3, and M-4 on the GPC column were 7.4, 7.4, 9.6, and 7.0 min, respectively. Since M-3 is similar in size to D-maltose and M-2, the longer retention time for M-3 suggests an attractive interaction between M-3 and the column matrix. We attribute this retarding force on the elution of M-3 to hydrophobic interaction between the hexamethylene segment of M-3 and the column matrix. On the other hand, the shorter retention time of M-4 is consistent with its larger molecular size compared with D-maltose. This result implies that the central, hydrophobic hexamethylene segment in M-4 is shielded from the column matrix by the two hydrophilic maltose units. This interpretation is consistent with similar GPC results we observed for the dextran polysaccharide surfactants.

The selective reaction of lactone with amine over hydroxyl groups assures a linear structure for both M-3 and M-4 products. A possible complication is reaction between lactone and hydroxyl groups. However, Kobayashi et al.[12,13] have demonstrated that lactones do not react with hydroxyl groups in refluxing methanol. Furthermore, if reaction between lactone and hydroxyl were to occur, it would produce high molecular weight poly(saccharide–ester), which was not observed in the GPC analysis of the product. In our analysis, the linear structures were further confirmed by ^{1}H-NMR. The ^{1}H-NMR spectra of D-maltose, M-3, and M-4 in DMSO-d_6 are shown in Figure 4. The proton peak due to the anomeric hydroxyl (6.67 ppm) in D-maltose is highlighted in the ^{1}H-NMR spectrum shown in Figure 4a.[15] The ^{1}H-NMR spectra of M-3 (Figure 4b) and M-4 (Figure 4c) show new proton peaks due to CONH (7.58 ppm), CONHCH_2 (3.09 ppm), and $(CH_2)_4$ (1.20–1.40 ppm), while the proton peak related to the anomeric position in maltose is absent. These proton peaks, which are indicative of successful reactions and purification, are also highlighted in Figure 8 for the analogous dextran surfactants. The only difference between the ^{1}H-NMR spectra of M-3 and M-4 is proton peaks derived from the hydrocarbon segments, that is, hexamethylene vs *n*-hexyl.

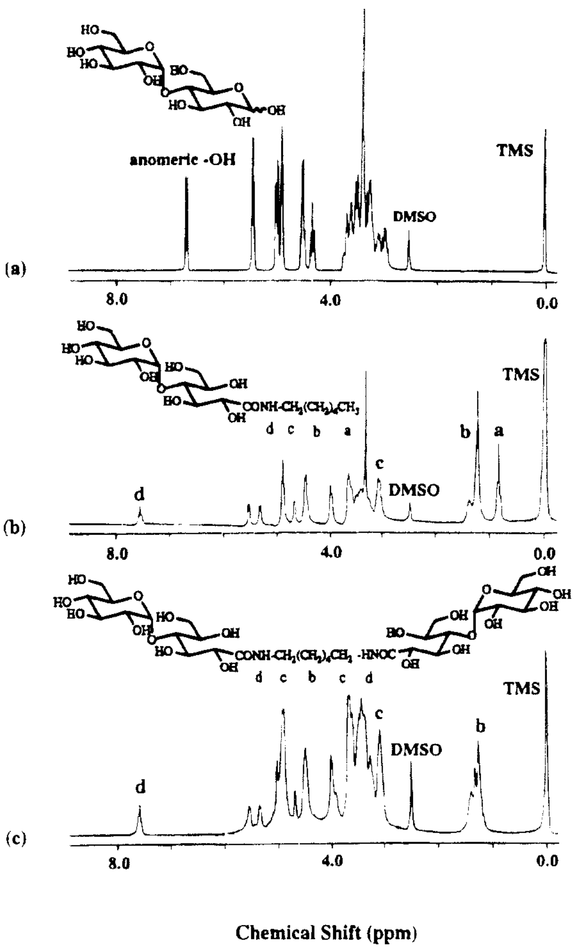


Figure 4. 200 MHz ^{1}H-NMR spectra of (a) D-maltose, (b), M-3, and (c) M-4 obtained in DMSO-d_6 at ambient temperature.

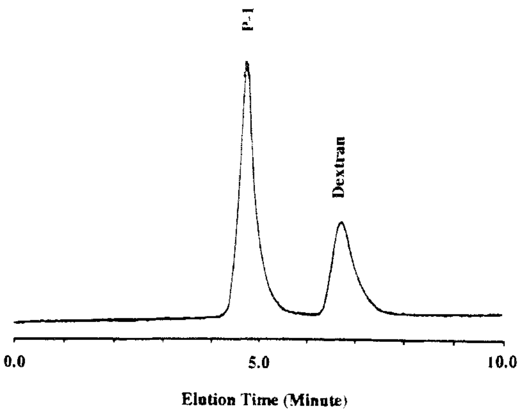


Figure 5. GPC trace of the dextran oxidation product after 2 h of reaction. GPC was carried out on a HEMA-BIO100 column at a flow rate of 1.0 mL/min using water as eluent.

Dextran Surfactants. The model compound studies provided very useful information. However, some adjustments to the reaction conditions were required for preparing the dextran surfactants, because of the low functional group concentration in dextran molecules. After 2 h, only 62% of the dextran was oxidized by I_2/KOH, as shown by the GPC trace (Figure 5). After 24 h, however, about 95% of the dextran was oxidized. A plot of the dextran oxidation conversion against reaction time is shown in Figure 6. The conversion increases steadily with reaction time and then levels off after 20 h. As with the model compounds, the dextran aldonic acid (P-1) was transformed into P-2 by lyophilization. It should be noted that D-maltose has α(1→4) glycosidic linkages while dextran has α(1→6) glycosidic linkages.

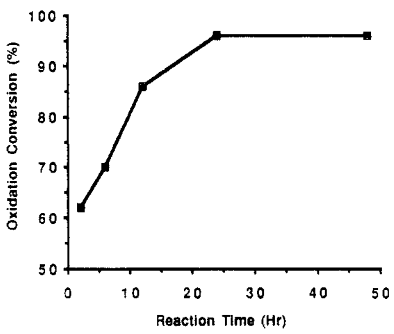


Figure 6. Plot of dextran oxidation conversion in percentage vs reaction time in hours.

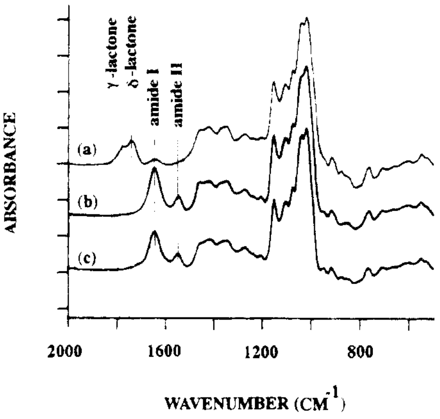


Figure 7. Transmission IR spectra (2000−500 cm^{-1} region) of (a) P-2, (b) P-3, and (c) P-4.

Therefore, only δ-lactone (1,5-lactone) can be formed from M-1, while both γ-lactone (1,4-lactone) and δ-lactone (1,5-lactone) can be formed from P-1. This distinction can be seen by comparing the IR spectrum of P-2 (Figure 7a) with the IR spectrum of M-2 (Figure 2). Only the ν(C=O) peak of δ-lactone at 1740 cm^{-1} is observed for M-2, while both the ν(C=O) peak of δ-lactone at 1745 cm^{-1} and the ν(C=O) of γ-lactone at 1771 cm^{-1} are present in the spectrum of P-2. In addition, P-2, like M-2, has some associated water, as indicated by the presence of a weak peak at 1620 cm^{-1}.

The diblock dextran surfactant (P-3) was synthesized by the reaction of dextran lactone (P-2) with hexylamine. A large excess of hexylamine (1/50 molar ratio of lactone to amine) was needed to drive the amidation reaction to completion. The IR spectrum of P-3 is shown in Figure 7b. The ν(C=O) at 1646 cm^{-1} and the δ(N−H) at 1547 cm^{-1} indicative of the amide bond (CONH) were both observed. During the time course of the reaction, the lactone peaks of P-2 at 1745 and 1771 cm^{-1} decreased, while the amide peaks at 1547 and 1646 cm^{-1} increased. The reaction was complete after 4 days at 60 °C, as shown by the disappearance of the two lactone peaks.

The triblock dextran surfactant (P-4) was synthesized by the reaction of dextran lactone (P-2) with 1,6-hexanediamine. In contrast to the reaction conditions used to prepare P-3, excess P-2 (2/1 molar ratio of lactone to amine was used to minimize monoamidation. In addition, an extended reaction time of 6 days at 60 °C was required to achieve significant conversion to P-4. The IR spectrum of P-4 is shown in Figure 7c. In following the reaction course by IR, we found that the δ-lactone peaks of P-2 at 1745 cm^{-1} decreased, while the amide peaks at 1547 and 1646 cm^{-1} increased with time. After 6 days of reaction, the δ-lactone peak of P-2 at 1745 cm^{-1} had disappeared while the γ-lactone peak at 1771 cm^{-1} was still present. This result suggests that the δ-lactone has higher reactivity than the γ-lactone. This is consistent with previous observations on the relative reactivities of δ- and γ-lactones in ring-opening reactions.[16]

The ion-exchange chromatography method developed for purification of the model compounds was adopted successfully for the purification of P-3 and P-4. The purity of both P-3 and P-4 after ion-exchange chromatography was approximately 98% as determined by GPC. The column retention times for dextran, P-2, P-3, and P-4 were 6.9, 6.9, 7.2, and 6.6 min, respectively. Analogous to our results for model compounds, the retention time of P-3 was longer than that of dextran and M-2, while the retention time of P-4 was shorter than that of dextran and P-2. We attribute the longer retention time of P-3 to hydrophobic interaction between the hexamethylene segment of P-3 and the column matrix. P-4 eluted according to its molecular size, because the hexamethylene segment was shielded by the two hydrophilic dextran chains. From the GPC data of the model compounds and dextran surfactants, it appears that the structure (diblock or triblock) of the surfactant plays a more important role in determining its GPC elution time than the hydrophilic to hydrophobic chain length ratio. If the hydrophobic segment is substituted by hydrophilic blocks at both ends (triblock), the hydrophobic interaction between the hydrophobic segment and the matrix is shielded and the surfactant is eluted according to its molecular size. This was observed in the case of M-4, which has only two short hydrophilic maltose blocks, and in the case of P-4, which has two dextran blocks attached to the hexamethylene segment. However, if the hexamethylene segment is substituted by a hydrophilic block at only one end (diblock), its elution through the column is retarded by the hydrophobic interaction. Again, this was observed for both the short-chain maltose surfactant (M-3) and the long-chain dextran surfactant (P-3).

The ^1H-NMR spectra of dextran, P-3, and P-4 are shown in Figure 8. The proton peak due to the anomeric OH (6.32−6.65 ppm) of dextran[15] is highlighted in Figure 8a. The proton peaks due to $CONH$ (7.82 ppm), $CONHCH_2$ (3.09 ppm), and $(CH_2)_4$ (1.20−1.40 ppm) were observed in the ^1H-NMR spectra of P-3 and P-4, while the proton peak due to the anomeric OH disappeared from these ^1H-NMR spectra.

The IR, GPC, and ^1H-NMR results indicate that our synthetic procedures and purification methods were successfully established to prepare novel diblock (AB type) and triblock (ABA type) polysaccharide surfactants with well-defined structure. This approach lays the groundwork for the preparation of more complex molecules, such as starlike and comblike polysaccharide surfactants. In addition, the composition and chain length of the polysaccharide surfactant molecules can be adjusted to provide a synthetic route for detailed examination of the adsorption behavior on solid surfaces, or alternatively, micelle formation in solution, the results of which can be used for correlation with theoretical prediction. The surface-active properties of these polysaccharide surfactants will depend on molecular geometry and the size of the hydrophobic segment. Surfactant properties as a function of hydrophobic chain length will be the subject of a future paper. Specifically, we envisage that this experimental approach will provide a practicable method for easily and dramatically modifying the surface properties of hydrophobic biomaterials and an opportunity to examine protein−surface interactions.

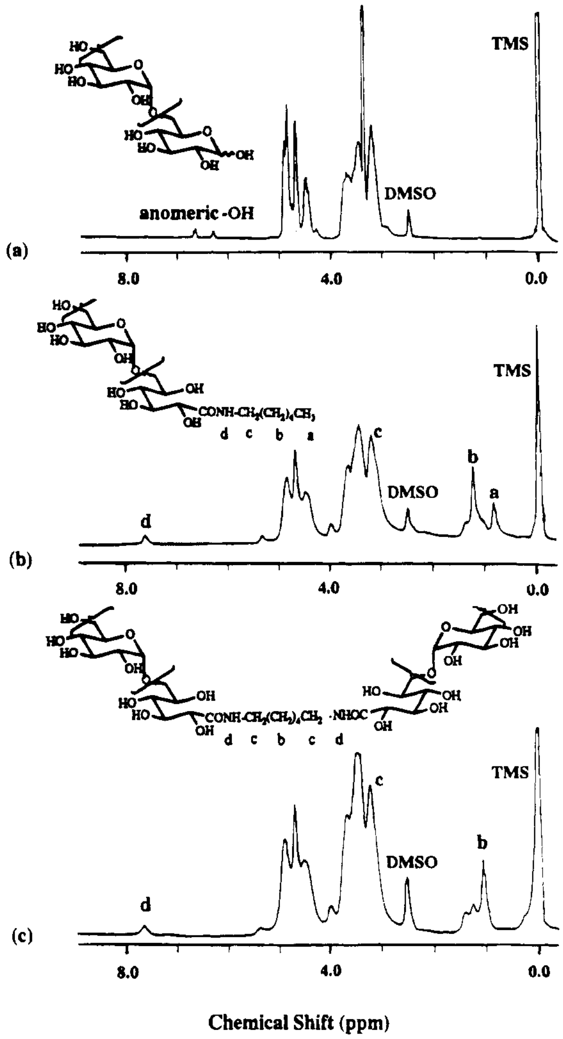


Figure 8. 200 MHz ^1H-NMR spectra of (a) dextran, (b) P-3, and (c) P-4 obtained in DMSO-d_6 at ambient temperature.

Conclusions

Novel diblock (AB type) and triblock (ABA type) dextran surfactants were synthesized, based on methods developed for corresponding model compounds from D-maltose. The linear structure of the polysaccharide surfactants was assured by the use of selective oxidation, lactonization, and aminolysis reactions. Ion-exchange chromatography was shown to be a useful purification method for the surfactants.

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