Controlled Synthesis of Poly(ϵ-caprolactone)-Grafted Dextran Copolymers as Potential Environmentally Friendly Surfactants

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ABSTRACT: The combination of bioresorbable and biodegradable hydrophilic polysaccharides with biodegradable hydrophobic polyester chains to form totally biodegradable, nonionic brushlike amphiphilic graft copolymers useful as surfactants has been investigated. In fact, a totally controlled and original three-step procedure is described which gives access to a wide range of poly(ϵ-caprolactone)-grafted dextran copolymer compositions. It consists of the reversible protection of the hydroxyl groups of the polysaccharide backbone by silylation, followed by the ring-opening polymerization of ϵ-caprolactone initiated by the free remaining hydroxyl groups of the partially silylated dextran in the presence of aluminum and tin-based catalysts. The last step relies upon the removal of silylating groups under mild acidic conditions yielding the desired amphiphilic graft copolymers.

Introduction

Recently, polymeric saccharide-based surfactants derived from block and graft copolymers have attracted much attention not only because of their potential in separation technologies and controlled drug release, but also because they offer a positive alternative to existing non biodegradable formulated systems.[1] However, most saccharide-based surfactants are based on mono- and disaccharides. Only few studies mention the use of polysaccharides as precursors of macromolecular amphiphilic architectures. For instance, brushlike poly(lactide)-grafted modified dextrans have been prepared by initiating lactide ring-opening polymerization (ROP) from some free hydroxyl groups of ionic polysaccharides in the presence of stannous octoate.[2] The synthesis of poly(lactide)-grafted pullulan from partially trimethylsilylated polysaccharides and subsequent initiation of the lactide ROP by potassium *tert*-butoxide have also been reported.[3] Finally, hydroxycellulose-grafted with poly(ϵ-caprolactone) has very recently been prepared by grafting ϵ-caprolactone on a film of polysaccharide by using pancreatic lipases.[4] Eventhough the aforementioned works have paved the way to new grafted architectures with promising properties, it is however worth pointing out that control of the polymerization in terms of grafting efficiency, graft length, content and distribution, and amphiphilicity has not been reported so far. The aim of this paper is thus to report on the controlled synthesis of poly(ϵ-caprolactone)-grafted dextran with a special emphasis on macromolecular characterization all along the synthetic procedure.

Very recently, some of us have demonstrated the great efficiency of aluminum alkoxides as initiator in ROP of ϵ-caprolactone (CL) in order to synthesize biodegradable compositions of corn starch and poly(ϵ-caprolactone) (PCL).[5,6] The ROP of CL has been carried out either in bulk (without solvent) or in 10 wt % toluene suspension from granular starch using the amylose/amylopectin hydroxyl functions after adequate activation into Al−alkoxides. These aluminum alkoxides have been in situ generated by reaction of triethylaluminum with hydroxyl functions available at the starch surface. XPS analysis has attested for the actual fixation of the aluminum active species on the starch surface, while good interfacial adhesion has been evidenced by SEM observations and enhanced thermomechanical properties. Growth of the polyester chains onto starch surface has been followed by laser light scattering granulometry.[6] In the present work, PCL-grafted dextran copolymers have been synthesized in a controlled way by using a three-step procedure. The proposed synthetic strategy involves the reversible protection of the polysaccharide hydroxyl functions and the ROP of ϵ-CL promoted by some remaining OH groups after activation into Al−alkoxides.

Experimental Section

Materials. Dextrans T10 and T40 were purchased from Pharmacia Biotech and dried under a reduced pressure of 0.06 mbar at 90 °C for one night and then at 120 °C for 5 h. Under above drying conditions, no degradation of the polysaccharide chains has been evidenced by size exclusion chromatography−low-angle laser light scattering (SEC−LALLS; see Characterization). 1,1,1,3,3,3-Hexamethyldisilazane (HMDS), triethylaluminum ($AlEt_3$) in solution in toluene (25 wt %) and stannous octoate ($Sn(Oct)_2$) were respectively purchased from Acros, Fluka, and Goldschmidt and used without any further purification.

After dilution with dry toluene, $AlEt_3$ and $Sn(Oct)_2$ solutions were stored in glass ampules under nitrogen. Triethylamine (99%) from Acros was dried over BaO for 72 h, distilled under reduced pressure and stored under nitrogen. ϵ-Caprolactone (CL) from Acros was dried over CaH_2 for 48 h, distilled under reduced pressure, and stored under inert atmosphere. Aluminum triisopropoxide ($Al(O^iPr)_3$) from Acros was distilled under reduced pressure in a previously flamed and nitrogen-purged conventional apparatus. Condensed at the temperature of liquid nitrogen, $Al(O^iPr)_3$ was allowed to warm to room temperature, rapidly dissolved in dry toluene and stored under

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Table 1. Dependence of Protection Yield and Substitution Degree (DS) on Dextran Molecular Weight and Silylation Experimental Parameters

entry	solvent (v/v)	[HMDS]/[OH]	*T* (°C)	*t* (h)	[NEt_3]/ [OH]	protection yield (%)	DS
1[a]	DMSO	2	50	16	0.0	77	2.3
2[a]	DMSO	2	50	16	0.4	87	2.6
3[a]	DMSO	4	60	48	0.2	87	2.6
4[a]	DMSO/THF (5:2)	4	60	48	0.2	92	2.8
5[a]	DMSO/THF (6:4)	4	80	90	0.2	100	3.0
6[b]	DMSO	2	50	16	0.0	71	2.1
7[b]	DMSO	8	20	16	0.0	89	2.7
8[b]	DMSO/THF (6:4)	4	60	48	0.2	100	3.0

[a] Dextran T10 with $M_n = 6600$ and $M_w/M_n = 1.6$ as determined by SEC in H_2O. [b] Dextran T40 with $M_n = 21\,300$ and $M_w/M_n = 1.8$ as determined by SEC in H_2O.

Table 2. Dependence of PCL-Grafted Silylated Dextran (Dextran T10) Composition on the Activator Nature and Polymerization Conditions (See Experimental Section)

	silylated dextran			activator					F_{PCL}			
sample	DS	M_n	$[CL]_0$/[OH]	nature	[Met]/[OH]	*t* (h)	*T* (°C)	f_{CL}	grav[b]	^{1}H NMR[c]	M_n[e]	M_w/M_n
1	2.6	12 600	20	$Al(Et)_3$	1.20	68	60	0.77	0.77	0.89	19 600	2.1[d]
2	2.8	10 100	20	$Al(Et)_3$	0.05	68	60	0.64	0.41	0.94	34 700	1.4
3	2.8	10 100	20	$Al(OiPr)_3$	0.02	68	60	0.64	0.20	0.16	11 600	1.2
4	2.6	12 600	20	$Al(OiPr)_3$	0.05	68	60	0.77	0.73	0.95	31 300	1.4
5	2.6	12 600	30	$Al(OiPr)_3$	0.05	68	60	0.83	0.77	0.95	28 300	1.3
6	2.7[a]	32 900	5	$Sn(Oct)_2$	0.05	44	100	0.32	0.26	0.39	34 300	1.6
7	2.7[a]	32 900	10	$Sn(Oct)_2$	0.05	44	100	0.50	ND	0.84	43 100	1.7
8	2.8	10 100	20	$Sn(Oct)_2$	0.05	68	100	0.64	0.50	0.84	36 500	1.5

[a] Dextran *T* 40 instead of dextran T10 (see Table 1). [b] PCL weight fraction in the copolymer as determined by gravimetry of the copolymer recovered after precipitation from heptane. [c] PCL weight fraction in the copolymer as determined by ^{1}H NMR from the relative intensities of the ester methylene protons, and the glucosidic methine and methylene protons in the range from 3.0 to 4.0 ppm, (see Experimental Section). [d] Bimodal SEC chromatogram. [e] Number-average molecular weight as determined by SEC in reference to a polystyrene calibration (see Experimental Section).

nitrogen atmosphere. The accurate solution concentration was determined by back complexometric aqueous titration of Al^{3+} with standard solutions of Na_2EDTA and $ZnSO_4$ at pH 4.8. Toluene and THF were respectively dried by refluxing over CaH_2 and Na/benzophenone complex and distilled just before use. DMSO was dried over molecular sieves 4 Å for 48 h, distilled under reduced pressure, and stored under nitrogen atmosphere.

Dextran Silylation. Dextran silylation was carried out in DMSO (10 wt % dried dextran) in a previously dried and nitrogen-purged round-bottom two-necked flask equipped with a stopcock and connected to an oil valve for ammoniac evolution. Once dextran was totally dissolved, desired amount of HMDS and triethylamine were added under a nitrogen flow with previously dried syringes. The reaction medium was kept at the desired temperature for a suitable period of time. In some cases, a given volume of THF was also added as soon as the reaction medium became cloudy. Silylated dextran solution was evaporated to dryness and the polymer recovered.

In those experiments in which THF was added to the reaction medium, silylated dextran was recovered by precipitation in heptane, filtration, and drying under reduced pressure.

Protection yield was calculated by ^{1}H NMR by using the following equation:

$$\text{yield (\%)} = \frac{I_{0.1\ \text{ppm}}}{27 \times I_{4.8\ \text{ppm}}} \times 100$$

ROP of CL from Silylated Dextran. The ROP of CL was performed in a previously dried two-necked round-bottom flask equipped with a stopcock and a rubber septum, purged with nitrogen, and kept at the desired temperature for a suitable period of time. Silylated dextran was first dried by three azeotropic distillations of toluene, then dissolved in dry toluene (10 wt % silylated dextran) and added with a defined volume of catalyst. When triethylaluminum was used as catalyst, the reaction flask was equipped with an oil valve for ethane evolution and the reaction stirred for 4 h at room temperature before adding CL and heating to 60 °C. A very similar procedure was used for $Al(O^iPr)_3$ except that three successive azeotropic distillations of toluene were performed to extract 2-propanol before monomer addition and to favor substitution reaction between alkoxide groups of $Al(O^iPr)_3$ and free hydroxyl functions remaining on silylated dextran. When $Sn(Oct)_2$ was used as catalyst, addition of $Sn(Oct)_2$ and CL were performed successively without any pretreatment, while the polymerization temperature was kept at 100 °C. Whatever the catalyst, the reaction product was recovered by precipitation in heptane, filtration, and drying under vacuum.

PCL weight fraction in the graft copolymers (F_{PCL}) was determined by either gravimetry after precipitation of the reaction product from heptane, or ^{1}H NMR spectroscopy as follows:

$$F_{PCL} = I_{PCL}MW_{CL} \Big/ \left\{ (I_{PCL}MW_{CL}) + \left(\frac{I_{\text{dextran}}}{3} [MW_{GL} + (DS \times MW_{\text{“SiMe}_3\text{”}}) + [(3 - DS) \times MW_{\text{“H”}}]] \right) \right\}$$

where I_{PCL} = ^{1}H NMR integral intensity of CL repeating units calculed from the average value as obtained from the methylene protons at 4.1 ppm (“$-CH_2-O-C(O)-$”) and 2.35 ppm (“$-O-C(O)-CH_2-$”), I_{dextran} = ^{1}H NMR integral intensity of glucosidic repeating units calculated from the methine and methylene protons in the range from 3.0 to 4.0 ppm; DS = degree of substitution by silylation; MW_{CL}, $MW_{\text{“SiMe}_3\text{”}}$, $MW_{\text{“H”}}$, and MW_{GL} are respectively, 114.1, 73.2, 1.0, and 159.1. MW_{GL} corresponds actually to one $C_6H_7O_5$ “deprotonated” glucosidic unit.

Deprotection of the PCL-Grafted Silylated Dextran. The protected graft copolymers were dissolved in THF (10 wt % PCL-grafted silylated dextran) along with the addition of a slight excess of HCl aqueous solution (1 M) with respect to the number of “$-O-Si(CH)_3$” functions.

After 2 h at room temperature, the deprotected copolymers were recovered by precipitation in heptane, filtration, and vacuum-drying. Note that sample 3 in Table 2, already precipitated directly from the THF solution after the deprotection step.

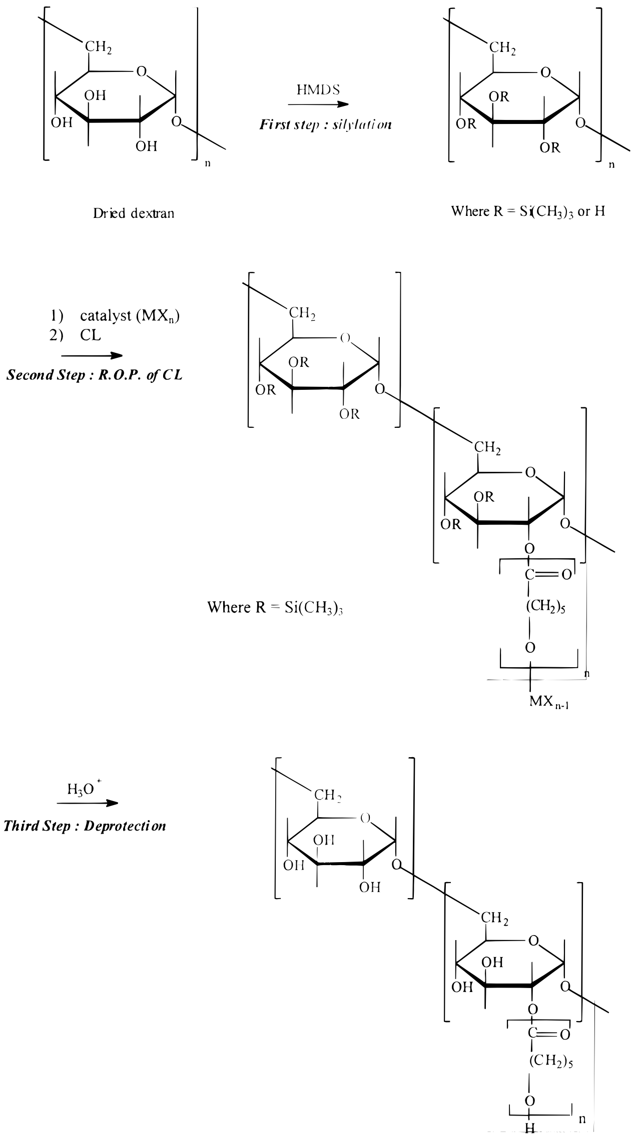
Characterization. ^{1}H NMR spectra were recorded using a Bruker AMX-300 apparatus in d_6-DMSO, $CDCl_3$, or d_8-toluene at various temperatures. Size exclusion chromatography (SEC) of silylated dextran and copolymers was performed in THF (sample concentration:1 wt %) at 35 °C using a Polymer Laboratory (PL) liquid chromatograph equipped with a PL-DG802 degazer, an isocratic HPLC pump LC1120 (flow rate: 1 mL/min), a Basic-Marathon Autosampler, a PL-RI refractive index detector, and four columns: a guard column PLgel 10 μm (50 × 7.5 mm) and three columns PLgel mixed-B 10 μm (300 × 7.5 mm). Molecular weight and molecular weight distribution were calculated by reference to a calibration curve built up by using polystyrene standards. SEC investigations of native dextrans were performed at room temperature using a Waters HPLC pump (Waters 410) equipped with a DG-1310 degazer, a serial set of SB-806-HQ, SB-805-HQ, SB-804-HQ OHPack columns and SB-OH Pack guard column (Shodex). Elution (0.7 mL/min) was dually monitored by low angles laser light scattering detection (Chromatix KMX 6, Milton Roy, USA) and differential refractometry (Waters 410). Refractive index increment equal to 0.146 was used. Native dextrans solutions (10 mg/mL) were prepared by dissolution in the aqueous eluent (0.1 M $NaNO_3$, 6.15×10^{-3} M NaN_3) and were left under vigorous stirring for 24 h. Filtration of the solutions thus prepared (Millex GSWP 0.22 μm) was carried out right before injection. FT-IR spectra were recorded using a BIO-RAD Excalibur spectrometer equipped with a ATR Harrick Split Pea. DSC measurements were performed under nitrogen flow by using a 2920 CE DSC apparatus from T. A. Instruments (heating rate: 10 °C/min). Melting and glass transition temperatures were recorded at the second scan. Some temperature modulated DSC (MDSC) were also carried out on the same apparatus with the following temperature modulation parameters: heating rate, 5 °C/min; modulation amplitude, 1 °C; and period, 60 s. Only the reversible heat flow recorded at the second scan is provided with. Dynamic surface tension measurements were carried out by using a Dataphysics OCA15 apparatus from THIS.

Results and Discussion

Dextran Silylation Reaction. The first step of the synthetic strategy depicted in Scheme 1 consists of protecting the hydroxyl groups of dextran by using 1,1,1,3,3,3-hexamethyldisilazane (HMDS) as silylating agent. The silylation of dextran is a direct route to reactive polysaccharide derivatives which possess a controlled number of free hydroxyl groups and which are soluble in a variety of organic solvents including toluene suited for carrying out the next step, i.e., ROP of CL. As our objectives are the synthesis of PCL-grafted dextran copolymers with amphiphilic properties, the target is to reach high degrees of hydroxyl protection so that a limited amount of PCL grafts can grow away from the remaining free alcohol functions. Protection yields higher than 85% will be focused on. Two polysaccharides characterized by different molecular weight have been studied, i.e., dextran T10 and T40 with M_n values of 6600 and 21 300, respectively.

Table 1 shows the main parameters affecting the protection yield of dextran chains. From the protection yield, one can readily calculate the degree of substitution (DS), i.e., the number of protected hydroxyl functions per glucosidic unit. The protection yield has been determined by ^{1}H NMR from the relative intensities of the trimethylsilyl groups at 0.1 ppm and the glucosidic protons multiplet centered at 4.9 ppm using $CDCl_3$ as solvent (see Experimental Section). As suggested by several authors,[7−9] this multiplet corresponds not only to the anomeric protons, but also to the hydroxyl protons of the glucosidic units. Such an assignment has been confirmed by adding D_2O to a native dextran solution in d_6-DMSO. Consequently due to the contribution of the remaining hydroxyl protons to the resonance multiplet at ca. 4.9 ppm, the lower the protection yield is, the more it is underestimated by ^{1}H NMR (by comparison of relative intensity at 0.1 and 4.9 ppm). However, at DS values higher than 2.6 which are our main target (vide supra), it comes out that this error becomes negligible compared to the ^{1}H NMR experimental error estimated at 10%.

Scheme 1



Even though the main objective of this work was not to investigate in detail the silylation reaction of dextran, as this study will be the object of another paper, Table 1 shows the possibility to tune up the degree of silylation by the experimental parameters. For instance, in the series of dextran T10 (entries 1−5), DS values ranging from 2.3 to 3.0, i.e., quantitative protection of polysaccharide chains, were obtained by modifying the HMDS content, reaction time, and temperature, as well as by addition of THF. The beneficial effect of the addition of THF during the course of the reaction can be explained by the change of the polysaccharide solubility in organic solvent as the silylation reaction proceeds. As an

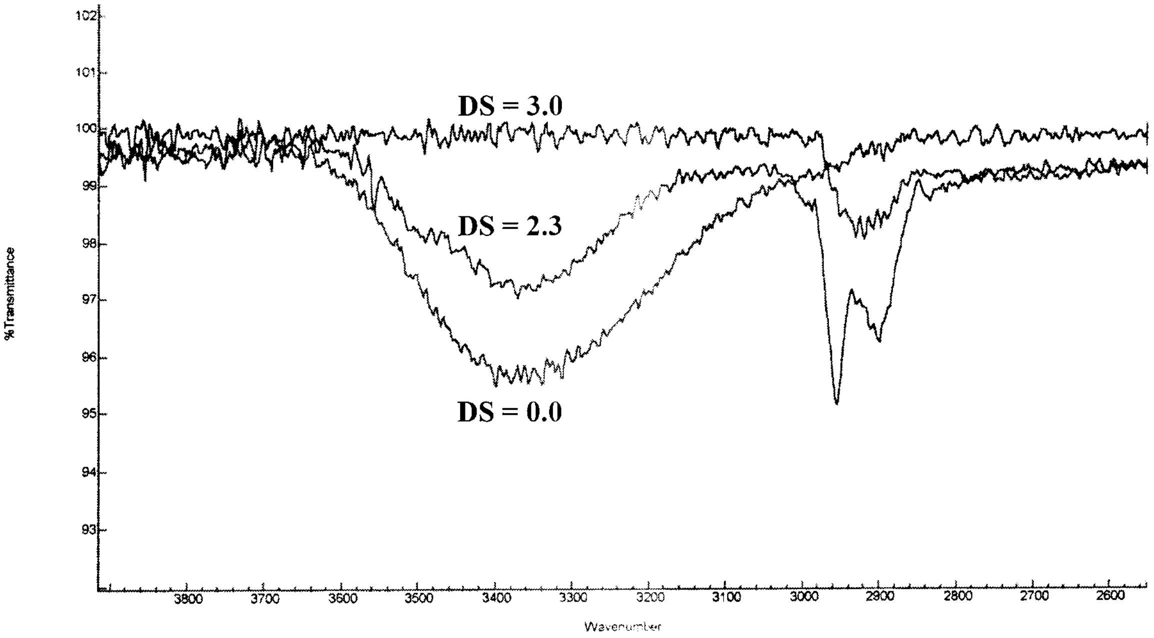


Figure 1. FTIR spectra of silylated dextrans with various DS.

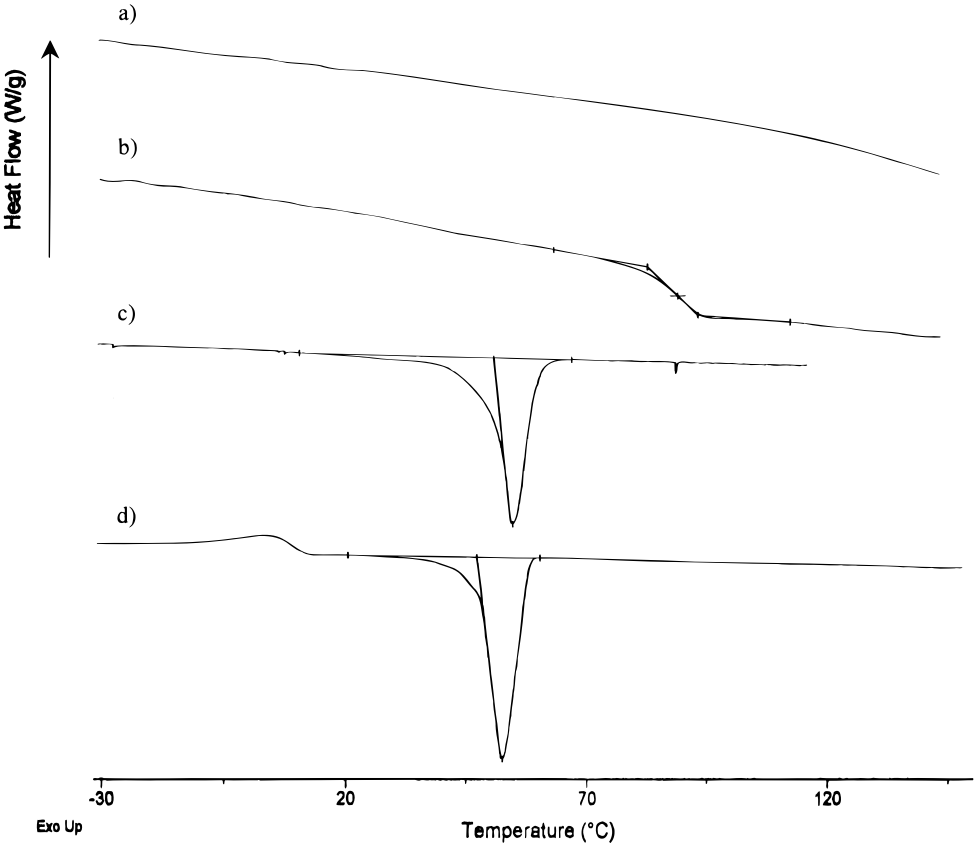


Figure 2. DSC thermograms of dextran T10 (a) before and (b) after the silylation step (with a DS of 2.8) and the resulting copolymer ($F_{\mathrm{PCL}} = 0.41$; sample 2 in Table 2) (c) before and (d) after the deprotection step (amphiphilic copolymer).

example, complete silylation of dextran T10 ($M_n = 6600$, entry 5) has been successfully achieved by using 4 equiv of HMDS and 0.2 equiv of triethylamine as an activator at 80 °C for 90 h in a final DMSO/THF (6/4 v/v) solvent mixture. Similar results have been obtained with dextran T40, which could be again fully silylated despite its rather high molecular weight (entries 6−8). The quantitative silylation of dextran is further evidenced by FT-IR spectroscopy (Figure 1) which displays the disappearance of a hydroxyl absorption band at ca. 3500 cm^{-1}. Six new absorptions related to the trimethylsilyl groups[10] can be detected at 750, 842, 874, 1020, 1156, and 1250 cm^{-1}. A systematic kinetic study of the silylation reaction of dextran covering a much wider range of DS will be reported soon.

Partially and totally silylated dextrans have been also characterized by temperature-modulated DSC (Figures 2 and 3). At the same level of silylation, polysaccharide chains with higher initial molecular weight (dextrans T40 compared to T10 for instance) display higher glass

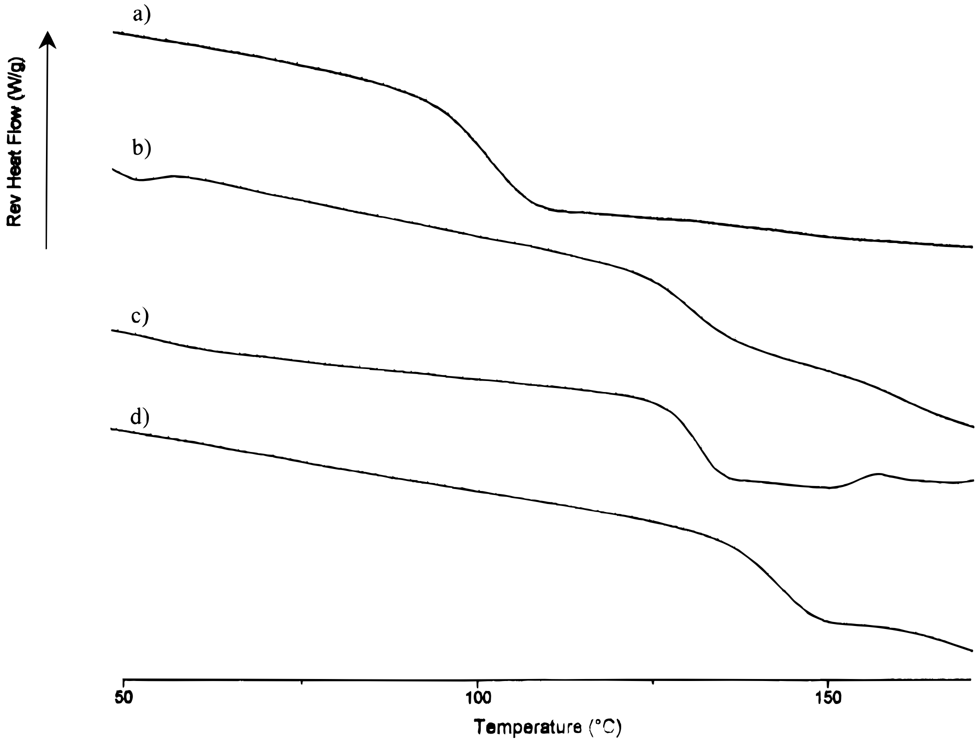


Figure 3. Temperature modulated DSC thermograms (reversible heat flow shown) of silylated dextrans with various DS: (a) dextran T10 with DS = 2.6 and dextran T40 with DS = 2.1 (b), 2.5 (c), and 3.0 (d).

transition temperatures T_g. At DS of ca. 2.5, dextrans T10 (with initial M_n = 6600) and T40 (21 300) are characterized by T_g at 91 and 131 °C, respectively (Figure 3, parts a and c). For the same native dextran, increasing the degree of silylation enhanced the T_g values (Figure 3, parts b−d). For instance, the fully protected dextran T40 (DS = 3.0) displays a T_g at 143 °C. It is worth mentioning that fully silylated dextran T10 behaves as a semicrystalline polymer with a melting endotherm at 183 °C (ΔH_m = 16.6 J/g, DSC not shown). The effect of molecular weight and silylation extent on the thermal behavior of the silylated dextrans deserves undoubtedly much more work to be fully understood. As it is out of the scope of the present investigation, this study will be the topic of a forthcoming paper.

ROP of CL from Silylated Dextran. The second step of the synthesis consists of the ROP of ϵ-caprolactone (CL) in toluene from the free remaining hydroxyl groups of the silylated dextrans, which were previously activated by either aluminum triisopropoxide ($Al(O^iPr)_3$), triethylaluminum ($Al(Et)_3$) at 60 °C, or stannous octoate ($Sn(Oct)_2$) at 100 °C (Table 2). At first, it must be emphasized that the PCL weight fraction in the graft copolymers (F_{PCL}) has been determined by either gravimetry after precipitation of the reaction product from heptane or ^1H NMR spectroscopy (Figure 4). It is worthwhile to point out that F_{PCL} was determined by ^1H NMR by comparison of the relative intensities obtained on one side from the average value calculated from the "$-CH_2-O(CO)$" ester methylene protons at 4.1 ppm and from the "$-O-C(O)-CH_2-$" α-carbonyl methylene protons at 2.35 ppm, and on the other side the glucosidic methine and methylene protons in the range from 3.0 to 4.0 ppm (see Experimental Section). Actually, ^1H NMR spectroscopy usually leads to F_{PCL} values higher than the gravimetric ones, more particularly for copolymers rich in PCL. F_{PCL} as determined by ^1H NMR can even exceed the initial feed weight fraction of CL (f_{CL}) as depicted in Table 2 (sample 8). Since some restriction of chain backbone mobility due to the numerous polyester grafts might be responsible for the partial screening of glucosidic protons in ^1H NMR spectra, measurements have been carried out at higher temperature. However, neither increasing temperature of the ^1H NMR analysis in $CDCl_3$ from 298 to 318 K nor substituting $CDCl_3$ for d_8-toluene at temperature up to 333 K provide better resolution of the polysaccharide sequence. This tends to indicate that the decrease of the transverse spin relaxation time of glucosidic protons cannot be easily overcome. Taking into account this observation, one may assume the formation of a quite stable core−shell cylindrical conformation as a result of the introduction of voluminous PCL grafts spread all along the silylated dextran backbone.

Therefore, higher PCL content will lead to overestimated F_{PCL} values measured by ^1H NMR spectroscopy, as is observed in Table 2. It is known that homopoly(macromonomer)s produce polymers exhibiting the conformation of highly dense cylindrical brushes, whereas graft copolymers yield, most of the time, macromolecules of spherical or starlike architecture.[12,13] Consequently, it seems that increasing the number and/or the length of the PCL graft segments in such a way that the polyester weight fraction (F_{PCL}) exceeds 0.3 might favor the formation of cylindrical-shaped macromolecules consisting of a silylated dextran inner core and PCL branches for the outer shell. To ensure that the covalent grafting of polyester sequences onto the silylated polysaccharide effectively affects ^1H NMR spectra, F_{PCL} has been determined for a sample blend prepared by mixing 30 wt % of silylated dextran (DS = 2.6) and 70 wt % of a homopoly(ϵ-caprolactone) (M_n = 5000) in $CDCl_3$. A F_{PCL} of 75 wt % has been calculated from the ^1H NMR spectrum recorded at room temperature, in good agreement with the expected value (within the experimental

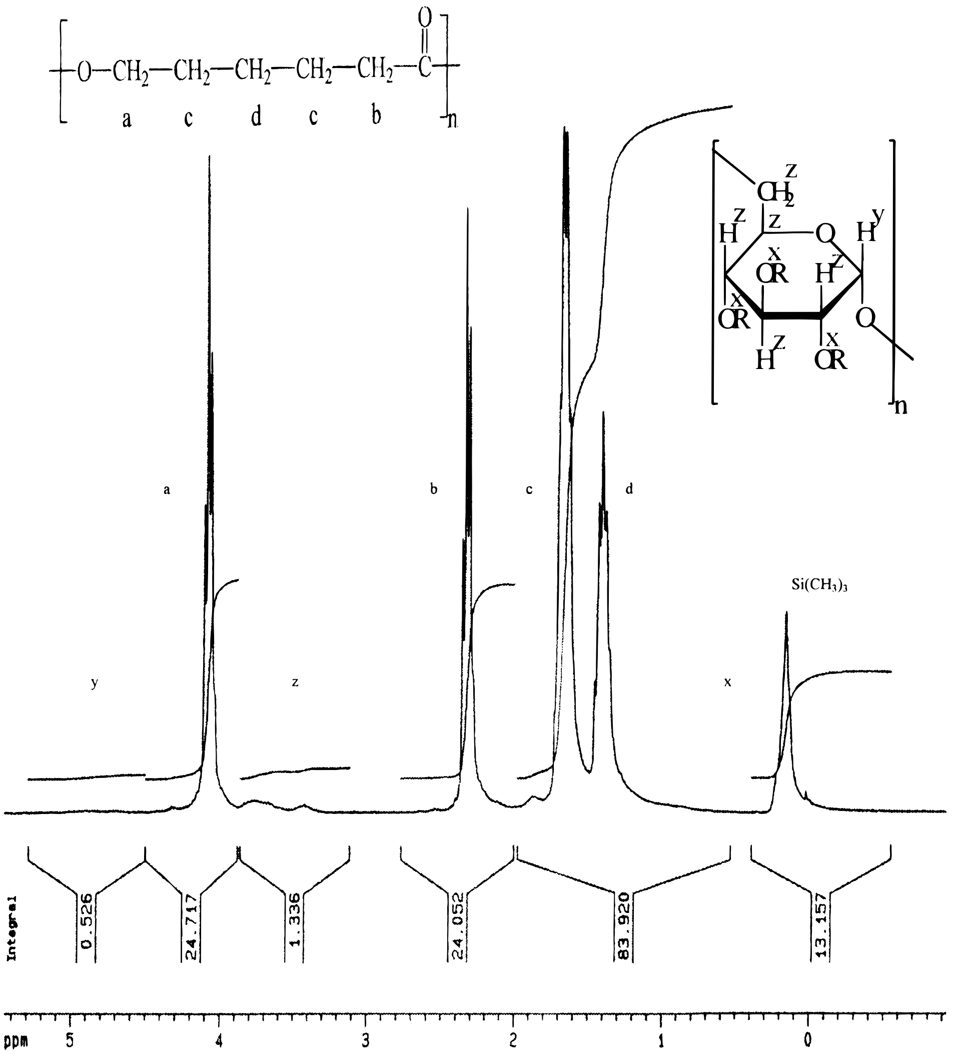


Figure 4. ^{1}H NMR spectrum of poly(ϵ-caprolactone)-grafted silylated dextran as obtained by ROP of CL from silylated dextran (DS = 2.8) added with $AlEt_3$ (solvent = $CDCl_3$ at room temperature, Table 2, sample 2).

Table 3. Length of PCL Grafts and Their Average Number Per Glucosidic Unit in the Silylated Dextran-Grafted PCL Copolymers

	silylated dextran						
sample	DS	M_n	$[CL]_0/[OH]$	F_{PCL}(grav)	conv (%)	DP_{PCL}[b]	N_g[c]
1	2.6	12 600	20	0.77	100	20	0.4
2	2.8	10 100	20	0.41	67	13	0.2
3	2.8	10 100	20	0.20	33	6.6	0.2
4	2.6	12 600	20	0.73	88	18	0.4
5	2.6	12 600	30	0.77	100	30	0.4
6	2.7[a]	32 900	5	0.26	100	5	0.3
8	2.8	10 100	20	0.50	83	17	0.2

[a] Dextran T40 instead of dextran T10 (see Table 1). [b] Degree of polymerization of PCL branches defined as the product of $[CL]_0/[OH]$ and copolymer conversion (x) (DP_{PCL} = $([CL]_0/[OH])x$). [c] Average number of PCL grafts per glucosidic units: N_g = 3-DS.

error of ^{1}H NMR analysis, i.e., ca. 10%). It can thus be concluded that gravimetry is better suited than ^{1}H NMR to determine F_{PCL}, especially when the initial CL weight fraction is higher than 0.3.

Interestingly, the good agreement between f_{CL} and gravimetric F_{PCL} shows that the experimental conditions allows one to reach high and, sometimes, even quantitative polymerization yields (Table 3). When $Al(Et)_3$ is used in slight excess with respect to the number of free hydroxyl groups remaining on the silylated dextran ($[AlEt_3]/[OH]$ = 1.2), the size exclusion chromatogram is bimodal (Table 2: sample 1). As reported by Penczek[14] and Teyssié,[15] alcohols readily react with $AlEt_3$ to form aluminum mono-, di-, and/or trialkoxides, depending on the reaction stoechiometry.

The as-obtained aluminum alkoxides are very efficient in initiating the ROP of lactones such as CL. It is well-known that some ethylaluminum dialkoxide might be produced together with the expected diethylaluminum monoalkoxide when triethylaluminum is reacted with an equimolar amount of alcohol. As previously reported by some of us,[16] the probability for ethylaluminum dialkoxide to be formed increases with the initial concentration of hydroxyl and the vicinity of these hydroxyl functions. Since ethylaluminum dialkoxide are more nucleophilic than diethylaluminum monoalkoxides, the initiation rate of the former is higher and consequently leads to macromolecules of a higher molecular weight. As a result, the coexistence of two different active species might be the primary cause for the bimodality. Some observations tend to support such an explanation. Indeed, it is worth mentioning that a rapid gelation of the reaction medium occurs which cannot be accounted for by coordinative interactions between aluminum alkoxide species but rather by primary covalent bonds. Indeed, gelation does not disappear upon addition of dry THF (a more polar

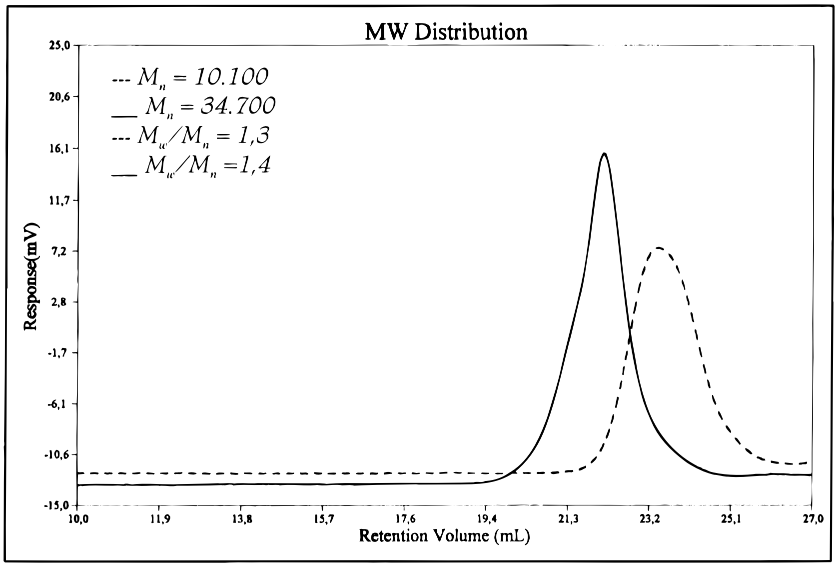


Figure 5. Size exclusion chromatograms of starting silylated dextran (- - -) and poly(ϵ-caprolactone)-grafted silylated dextran (—) as obtained by ROP of CL for a [Al]/[OH] molar ratio of 0.05 (Table 2, sample 2).

solvent than toluene), but does upon addition of a diluted aqueous solution of HCl which hydrolyzes the "Al−O" linkages. This is totally consistent with the simultaneous formation of ethylaluminum dialkoxides acting as cross-links and diethylaluminum monoalkoxides. In contrast, when a catalytic amount of $AlEt_3$ ([Al]/[OH] = 0.05) is used to initiate the ROP (Table 2, sample 2), the polymerization of CL is slower but the molecular weight distribution is monodisperse ($M_w/M_n = 1.4$) and narrower (Figure 5). Such a behavior can only be explained by a fast rate of alcohol−alkoxide interchange compared to the propagation rate so that only one type of active aluminum alkoxide actually initiates and propagates the ROP.

It has been widely reported that when aluminum trialkoxides are used as initiators, the polymerization of lactones, lactide, glycolide, and cyclic anhydrides proceeds via a controlled/"living" coordination−insertion mechanism, at least within the time required to reach quantitative monomer conversion.[17] In this study, $Al(O^iPr)_3$ has been used as a catalyst, i.e., in large default with respect to the number of free hydroxyl group remaining on the silylated dextran. Owing to the fast alcohol−alkoxide interchange compared to the propagation rate, such conditions have been previously shown to decrease the occurrence of transesterification reactions, while the molecular weight of the growing chains can be predetermined by the total number of hydroxyl and alkoxide functions.[17] From Tables 2 and 3 (samples 3−5), it can be seen that increasing the initial $[Al(O^iPr)_3]/[OH]$ molar ratio from 0.02 to 0.05 allows to enhance the propagation rate so that complete monomer conversion can be reached within 68 h at 60 °C ($F_{PCL} \sim f_{CL}$). Furthermore, the molecular weight distribution is monodisperse and narrow ($1.2 \le M_w/M_n \le 1.4$). Finally, despite its tendency to promote more side reactions than aluminum alkoxides, stannous octoate which is widely used as a catalyst in lactones ROP, has been also used to promote the ROP of CL at 100 °C from the partially silylated dextran. The results are very similar to those obtained by using $Al(O^iPr)_3$ at 60 °C, except for the copolymer polydispersity which is between 1.5 and 1.7.

Since the architecture and composition of the resulting graft copolymers might be different, it is hazardous to draw conclusions about the observed polydispersity increase. Furthermore, solvent fractionation experiments achieved on the crude polymerization products have also confirmed the absence of homopoly(ϵ-caprolactone). On the basis of these data, it can be stated that the grafting efficiency, defined as the weight ratio of the grafted polymer over the total polymerization product, is close to 1. So, assuming that each free remaining hydroxyl group of the silylated dextran effectively initiates the ROP of CL and that the usually met "living" character of the so-called "coordination−insertion" mechanism is preserved,[17] the average length of every PCL branch (DP) can be calculated, as well as the average number of grafts per glucosidic unit (N_g) (Table 3). On that basis, it is interesting to note that the cylindrical-shaped conformation, which has been attributed to graft copolymers displaying some discrepancy between F_{PCL} obtained by gravimetry and ^1H NMR spectroscopy, is formed not only for a PCL weight fraction (F_{PCL}) higher than 0.3 but particularly for a longer PCL chain length, i.e., for higher DP_{PCL}. In contrast, more flexible and mobile copolymer conformations are obtained when the PCL chain length is limited to low polymerization degree (samples 3 and 6).

Deprotection of the PCL-Grafted Silylated Dextran. The third step of the synthesis consists of the removal of the trimethylsilyl protecting groups by treatment of the graft copolymers in THF solution with a slight excess of an aqueous HCl solution. Complete deprotection has been demonstrated in FT-IR spectroscopy by the disappearance of absorption bands of trimethylsilyl functions at the benefit to a large absorption at ca. 3500 cm^{-1} typical of hydroxyl groups (Figure 6). As expected the six absorption bands related to the trimethylsilyl groups at 750, 842, 874, 1020, 1156, and 1250 cm^{-1} have disappeared.

From the ^1H NMR spectrum in d_6-DMSO at 310 K, no trimethylsilyl protons could be detected at 0.1 ppm anymore. Furthermore, both glucosidic and polyester protons are observed, at least for an initial PCL weight fraction of 0.3 and/or a DP_{PCL} of 5. Indeed, similar to the previously discussed PCL-grafted silylated dextran, the glucosidic protons of deprotected dextran component remain again poorly resolved, particularly when the

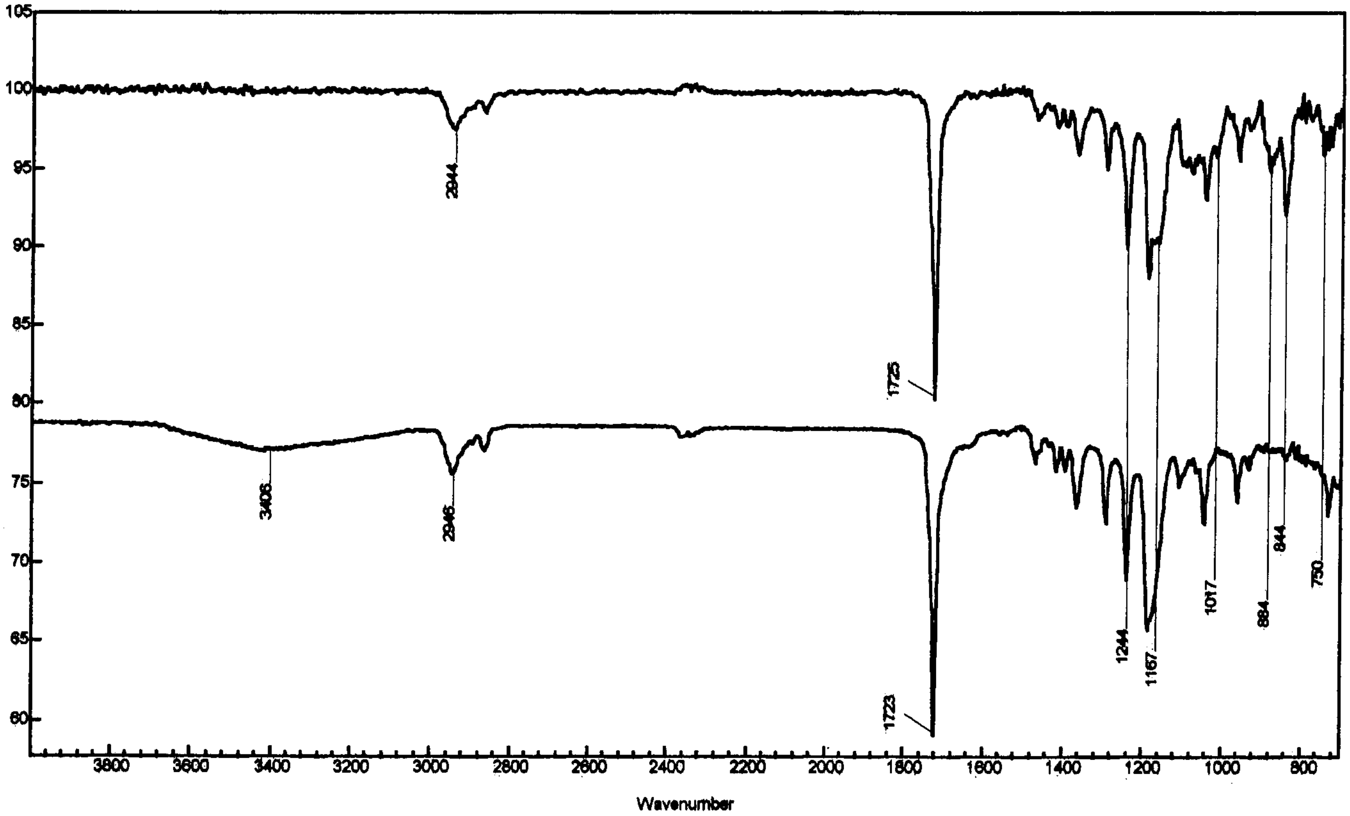


Figure 6. FTIR spectra of protected and deprotected grafted copolymers (Table 2, sample 2).

relative content and/or the length of polyester grafts increase. This could indicate that the cylindrical-shaped conformation proposed for PCL-grafted silylated dextran with F_{PCL} higher than 0.3 is maintained after hydroxyls deprotection of the polysaccharide backbone. The deprotected PCL-grafted dextran remains hygroscopic as attested by the high difficulty for extracting water molecules, the protons of which contaminate the ^{1}H NMR spectrum (broad resonance signal at ca. 3.8 ppm). It is worth pointing out that both protected and deprotected PCL-grafted dextrans are semicrystalline with a melting temperature attributed to the PCL grafts at ca. 57 °C (ΔH_m = 58.1 J/g), as determined by DSC (Figure 2d).

The solubility behavior of the copolymers strongly depends on the relative content in PCL grafts. As expected, limited solubility in water solution was observed for high PCL content. Contrarily copolymers characterized by low F_{PCL} values were rather insoluble in organic solvent such as toluene or THF. It is worth pointing out that deprotected PCL-grafted dextran copolymers proved to be only soluble in DMSO at 50 °C. To get a better insight into the potentialities of deprotected PCL-grafted dextran as surfactants, a preliminary study of surface tension in aqueous solution has been carried out. For that purpose, a graft copolymer characterized by a F_{PCL} of 0.2 (before OH deprotection) and a DP_{PCL} of 6.6 (sample 3 in Tables 2 and 3) has been studied. Surface tension expressed in mN/m has been determined by the pendant-drop method. Compared to pure water and dextran T10 aqueous solutions, the surface tension of the copolymer aqueous solution drops from 73 down to 54 mN/m for a concentration of 5 g/L. Therefore, PCL-grafted dextran amphiphilic copolymers display promising surfactant properties.

Further detailed dynamic surface tension experiments carried out with copolymers of different compositions and molecular weight are under current investigations and will be the topic of a forthcoming paper.

Conclusions

A three-step procedure has been proposed to control the synthesis of poly(ϵ-caprolactone)-grafted dextran amphiphilic copolymers. It consists of the reversible protection of the hydroxyl groups of the polysaccharide backbone by silylation, followed by the ring-opening polymerization of ϵ-caprolactone initiated by the free remaining hydroxyl groups of the silylated dextran.

The third and final step involves the polysaccharide hydroxyl deprotection under very mild conditions. The high efficiency of grafting and the control over the grafts molecular weight and molecular weight distribution rely upon the well-known “living” nature of the coordination-insertion mechanism of the ring-opening polymerization that is initiated by aluminum alkoxides. Accordingly, the free hydroxyl groups remaining along the polysaccharide backbone have been activated by using either $AlEt_3$ or $Al(O^iPr)_3$ in catalytic amount so as aluminum alkoxides are made available and can interchange quickly with remaining free hydroxyl groups, compared to the propagation rate. Tin octoate has also proved to be a good catalyst even though the polydispersity of recovered grafted copolymers was a little broader. The characterization of the graft copolymers by ^{1}H NMR spectroscopy has highlighted that the graft copolymer can adopt a core−shell cylindrical-shaped conformation, particularly at high weight fraction of hydrophobic polyester branches and/or high degree of polymerization of poly(ϵ-caprolactone). Preliminary dynamic surface tension experiments have shown the potential of those amphiphilic graft copolymers as surfactants. Further studies concern the incorporation of such biodegradable aliphatic polyester-grafted dextran in formulation of drug delivery systems.

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