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Partial or total silylation of dextran with hexamethyldisilazane

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Abstract

The silylation reaction of dextran with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) in DMSO was studied as the first step of the synthesis of new amphiphilic polyester-grafted dextrans. According to the experimental conditions, i.e. dextran molar weight, medium temperature and reaction time, HMDS/OH ratio, addition of a catalyst and co-solvent, partially or totally silylated dextrans were recovered. The highest silylation yields were obtained with the lowest molecular weight dextrans. The increase in temperature medium and/or reaction time, the presence of catalyst or co-solvent favored the protection yield. Whatever the dextran used, complete silylation of the polysaccharide chain could be achieved by adequate selection of the experimental conditions. The thermal properties of resulting silylated polysaccharides were investigated by temperature modulated DSC. It was observed that T_g values of partially silylated dextran were maintained between 120 and 140 °C, independently of the dextran molecular weight. Interestingly, DMSO proved to behave as an efficient plasticizer of (partially) silylated dextrans. The partially silylated dextrans were efficiently used as multifunctional macroinitiators for the controlled ring-opening polymerization (ROP) of lactone. The ROP was then promoted from the remaining hydroxyl groups in the presence of tin or aluminium activator. After polymerization and ultimate deprotection of the silylated dextran backbone, amphiphilic polyester-grafted dextrans were readily recovered.

Keywords: Polysaccharide modification; Polyester-grafted dextran; Amphiphilic copolymer

1. Introduction

Depending on their hydrophobic lipophilic balance numbers [1] typical applications of amphiphilic copolymers vary from emulsifier to detergent or solubilizer. But at present, public health and environmental regulations urge people to use non-toxic materials.

For a few years, polysaccharide-based surfactants have attracted much attention. However, only few studies report about the synthesis (most often with a limited control) of totally biodegradable polysaccharide-based amphiphilic copolymers [2–8]. In this regard, various polysaccharides have been studied such as pullulan, amylose, starch, dextran, etc. Among them, the latter deserves a special attention from a biomedical application viewpoint [9,10]. Dextrans are polysaccharides synthesized from sucrose by microorganisms. The most studied dextrans are produced by *Leuconostoc mesenteroides* [11], strain B-512(F) and hydrolyzed under acidic conditions in a controlled way. The resulting linear polysaccharides consist of α-D glucose units having preponderant α(1 → 6) glucosidic linkages (Fig. 1), while few percents of (1 → 3) glucosidic linkages provide side chains. A large number of these branches appear to be short.

Recently we published the first controlled synthesis of poly(ε-caprolactone)-grafted dextran (PCL-grafted dextran) [12] from partially trimethylsilylated dextrans and initiation of the ε-caprolactone (CL) ring opening polymerization (ROP) by aluminum alkoxides along the polysaccharides chains. The strategy used for the synthesis of such a copolymer is depicted in Scheme 1. In fact, the preparation of polyester-grafted dextran is made difficult because of the different nature of polyester chains (hydrophobic) and of dextran (highly hydrophilic). Therefore, to prevent the cyclic ester ROP from occurring under heterogeneous conditions, which is not favorable for getting high polymerization yield, one can make dextran partially hydrophobic so that the ROP could be performed under homogeneous conditions in an appropriate organic solvent. Partial hydrophobization of dextran can be achieved for example by a controlled silylation reaction, i.e. leading to a silylated

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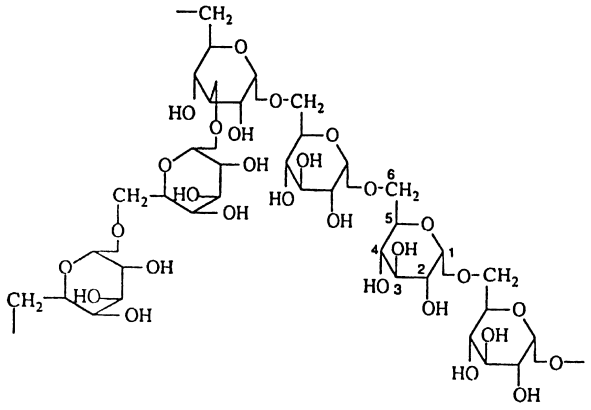
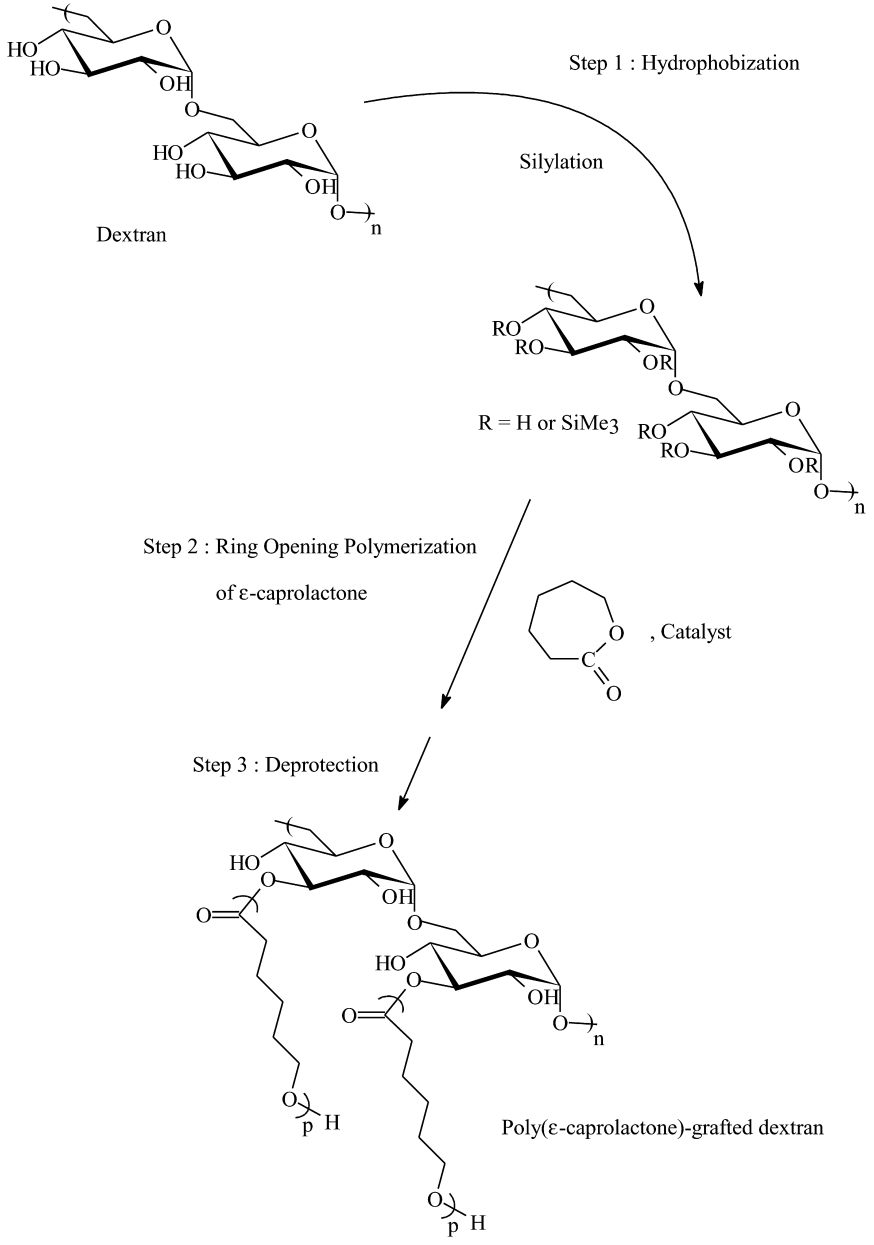


Fig. 1. Dextran structure.

polymer possessing a controlled number of residual free alcohol functions available for further ROP of cyclic ester (Scheme 1).

This paper aims at reporting for the first time at least at the best of our knowledge on the in-depth study of the partial or total silylation of dextran polysaccharide chains using 1,1,1,3,3,3-hexamethyldisilazane (HMDS). Influence of various parameters on the silylation yield (i.e. the degree of protection) was investigated. Parameters such as molar mass of initial dextran, temperature medium and reaction time, HMDS/OH ratio, addition of a catalyst and of a solvent of silylated dextrans were studied. The second part of this paper will be devoted to the thermal properties of the silylated dextrans. Some results on the controlled synthesis of polyester-grafted dextrans, according to the strategy



Scheme 1. Strategy of poly(ε-caprolactone)-grafted dextran synthesis.

given in Scheme 1, will be rapidly reported in the last part of this paper.

2. Experimental part

2.1. Materials

Dextrans T10 and T40 were purchased from Pharmacia Biotech and dried under a reduced pressure at 100 °C for one night. Three dextrans characterized by different molar masses were used, i.e. dextran T10 with $\overline{M_n}$ of 6600 g mol^{-1} (D_{10}) and two different batches of dextran T40 noted in the following text D^1_{40} and D^2_{40} with $\overline{M_n}$ of 31,000 g mol^{-1} and $\overline{M_w}$ of 40,000 and 38,000 g mol^{-1}, respectively. No degradation of the polysaccharide chains was evidenced either under the above drying conditions or along the silylation reactions (vide infra) as attested by size exclusion chromatography coupled to a multi-angle laser light scattering detector (SEC-MALLS). HMDS (99.9%) and chlorotrimethylsilane (TMSCl) (99%) were purchased from Aldrich and were used without any further purification. Triethylamine (99%) from Fluka was dried over BaO for 72 h, distilled under reduced pressure and stored under nitrogen.

Toluene and dimethylsulfoxide (DMSO) were refluxed over CaH_2, and tetrahydrofuran (THF) over Na/benzophenone complex. After distillation, solvents were stored under nitrogen atmosphere. Just before use, toluene, DMSO and THF were further dried over polystyryl lithium, CaH_2, and Na/benzophenone complex, respectively, and were distilled again.

2.2. Dextran silylation

Silylation was carried out in DMSO in a previously dried and nitrogen purged round bottom two-necked flask equipped with a stopcock. Once 1 g of dried dextran was totally dissolved in 30 ml of DMSO, desired amount of silylating agent and triethylamine (when necessary) 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, given volumes of THF or toluene were also added after 4 h of reaction. The medium was concentrated and the expected silylated dextran was recovered by precipitation. Depending on the initial dextran used, precipitations of silylated dextran were performed from heptane or cooled water (no hydrolysis of the $-OSiMe_3$ groups was evidenced during the precipitation step).

2.3. Silylation yields

Protection yields were calculated by ^{1}H NMR in $CDCl_3$ or in d_6-DMSO depending on the extent of silylation. Highly silylated dextrans were soluble in $CDCl_3$ while slightly silylated dextrans were soluble in D_2O or d_6-DMSO. In case of slightly silylated dextrans, similar silylation yields were obtained in D_2O and d_6-DMSO.

Silylation ratios were calculated using Eqs. (1) and (2)

$$\text{yield}(\%) = \frac{A_{\text{OSiMe}_3}}{A_{\text{anomeric H}}}\frac{100}{27} \quad (1)$$

or

$$\text{yield}(\%) = \frac{A_{\text{OSiMe}_3}}{A_{\text{glucosidic H}}}\frac{6\times 100}{27} \quad (2)$$

where A_{OSiMe_3}, $A_{\text{anomeric H}}$ and $A_{\text{glucosidic H}}$ are the respective areas of the trimethylsilyl group (at 0.15 ppm in $CDCl_3$ or 0.18 ppm in d_6-DMSO), of the anomeric protons centered at 4.7 ppm in $CDCl_3$ or d_6-DMSO, and of the glucosidic protons from 3.2 to 4.2 ppm in $CDCl_3$ or from 3.0 to 4.0 ppm in d_6-DMSO, respectively, (Fig. 2). Similar protection yields were obtained regardless of Eq. (1) or Eq. (2).

As suggested by several authors [13–15], the multiplet centered at 4.7 ppm in d_6-DMSO corresponds not only to the anomeric protons, but also to the hydroxyl protons of the glucosidic units. Such an assignment was confirmed by adding D_2O to a dextran solution in d_6-DMSO. Consequently due to the contribution of the remaining hydroxyl protons to the resonance multiplet at ca. 4.7 ppm, the lower the protection yield, the more it is underestimated by ^{1}H NMR (by comparison of relative intensity at 0.18 and 4.7 ppm). However, at higher silylation yield, it is noted that this error becomes negligible compared to the ^{1}H NMR experimental error.

Confirmation of the protection yields was obtained after reaction between the remaining free OH functions in partially silylated dextran with an excess of phenylisocyanate out in THF at 40 °C with 0.2 mol of NEt_3 per mol OH [16]. The relative content of the so-obtained phenyl carbamate functions as measured by ^{1}H NMR, either before or after hydrolysis of the $-OSiMe_3$ groups, strictly confirm the protection yield initially calculated from Eqs. (1) and (2).

From these data, one can readily determine the degree of substitution (DS), i.e. the number of protected hydroxyl functions per glucosidic unit. DS was calculated from the silylation yield using Eq. (3):

$$\text{DS} = \frac{3\text{yield}(\%)}{100} \quad (3)$$

2.4. ROP of cyclic ester from silylated dextran

As previously described [12], a partially silylated dextran was first dried by three azeotropic distillations of toluene, then dissolved in dry toluene. A defined volume of catalyst was then added to the resulting solution followed by the addition of CL or D,L-lactide (LA) toluene solution. Polymerization temperature was kept at the desired value for a suitable period of time. The reaction product was recovered

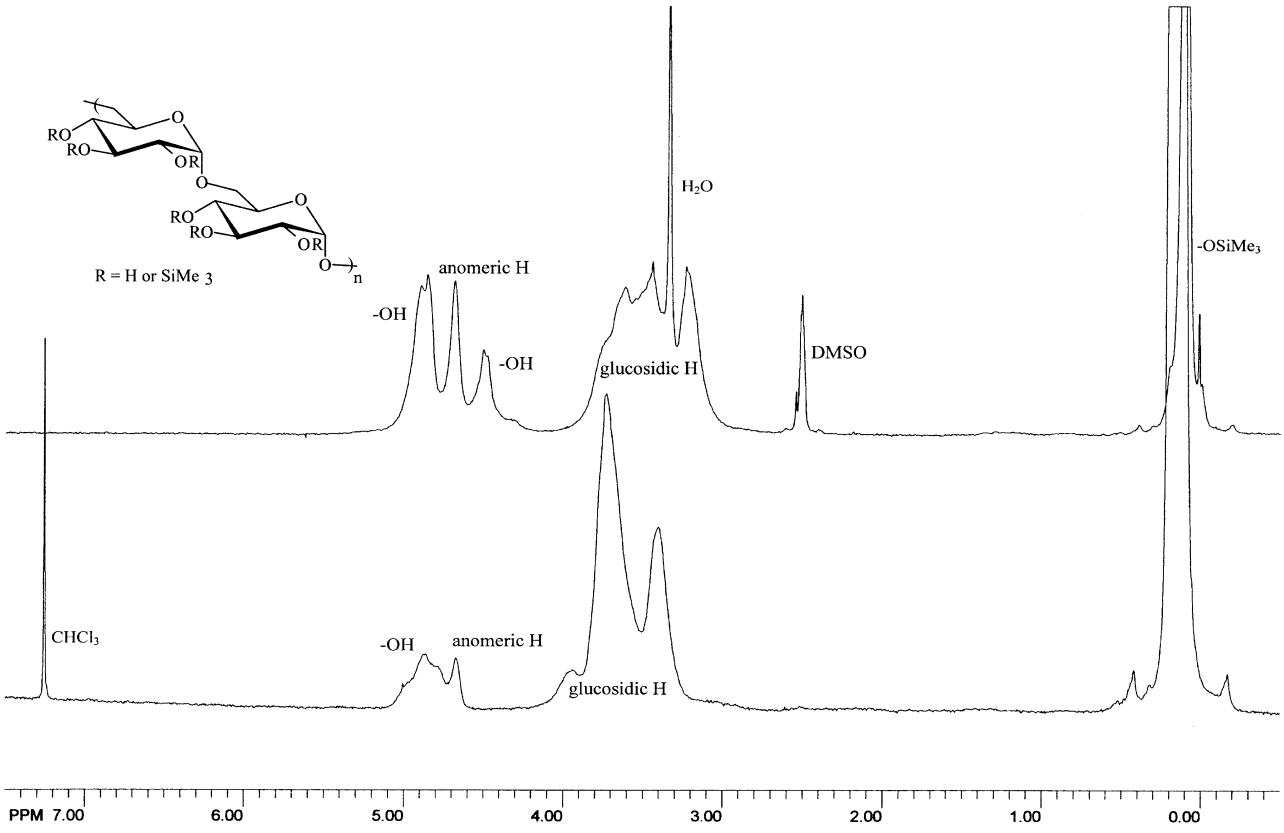


Fig. 2. ^{1}H NMR spectra of (partially) silylated dextrans in d_6-DMSO (upper) and in $CDCl_3$ (down).

by precipitation in heptane, filtration and drying under vacuum.

2.5. Deprotection of the polyester-grafted silylated dextran

As previously described [12], the silylated graft copolymers were dissolved in THF and a slight excess of HCl aqueous solution (1 M) with respect to the number of '–O–Si(CH)$_3$' functions was then added. After 2 h at room temperature, the deprotected copolymers were recovered by precipitation in heptane, filtration and drying under vacuum.

2.6. Characterization

^{1}H NMR spectra were recorded using a Bruker AC 200-P apparatus in d_6-DMSO, $CDCl_3$ or D_2O. Size exclusion chromatography (SEC) of silylated dextran was performed in THF (sample concentration: 1 wt%) at room temperature using a Merck HPLC pump (L-6200A) equipped with a degazer, two columns PLgel mixed D 5 μm (300×7.5 mm^2) and PLgel 5 μm (50×7.5 mm^2) guard column (Polymer Laboratories). Elution (0.7 ml min^{-1}) was dually monitored by multi-angle laser light scattering detection (MALLS) and differential refractometry (Merck RI-71). SEC of initial dextrans was 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^{-1}) was dually monitored by MALLS and differential refractometry (Waters 410). A refractive index increment of 0.146 was used. Initial dextran solutions (10 mg ml^{-1}) 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.

DSC measurements were performed under nitrogen flow by using a 2920 CE Modulated DSC apparatus from T.A. Instruments (heating rate: 5 °C min^{-1}; modulation of amplitude: 1 °C and period: 60 s). Glass transition temperatures were recorded at the second scan.

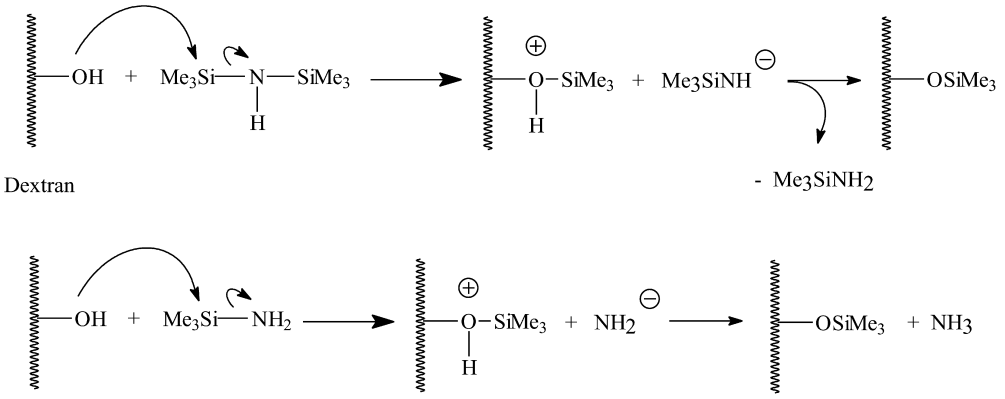
FT-IR spectra were recorded using a BIO-RAD Excalibur spectrometer equipped with a ATR Harrick Split Pea™.

3. Results and discussion

3.1. Silylation reaction of dextran

As hydrophobization step in Scheme 1, the silylation reaction was chosen since it exhibits many advantages:

- Fast and quantitative silylation of glucosidic unit [17].
- Stability of resulting silylether under basic conditions.



Scheme 2. Silylation mechanism with HMDS.

That will allow the pseudo anionic (coordination-insertion) ROP of the cyclic ester.

- Silylation of dextran chains produces a decrease in chain polarity. Thus (partially) silylated dextrans are soluble in THF or toluene which are suited for the subsequent ROP.
- Easy deprotection of $-OSiMe_3$ groups by acid hydrolysis or Bu_4NF treatment. This deprotection step achieved after the ROP of cyclic ester restores the hydrophilicity of dextran backbone, which is needed to produce polyester-grafted dextrans with amphiphilic properties.

Silylation of polysaccharides has been typically achieved with HMDS [18] or chlorotrimethylsilane (TMSCl) [19] generating NH_3 or HCl, respectively, or with a mixture of HMDS and TMSCl [20]. Use of TMSCl requires a base to neutralize the generated HCl and pyridine is usually used for this purpose. In all the aforementioned works [18–20], the silylation reaction was performed under heterogeneous conditions as the used polysaccharides were insoluble in pyridine [19,20] or formamide [18]. Complete silylation [15] was only observed in case of amylose, cellulose and pullulan. This reflects the difference in chemical reactivity existing in the polysaccharide family with strong effect of the intimate chemical composition and glucosidic units enchainment. Complete silylation of cellulose [21–23] in ammonia was recently reported. To the best of our knowledge, the complete silylation of dextran has not been reported so far.

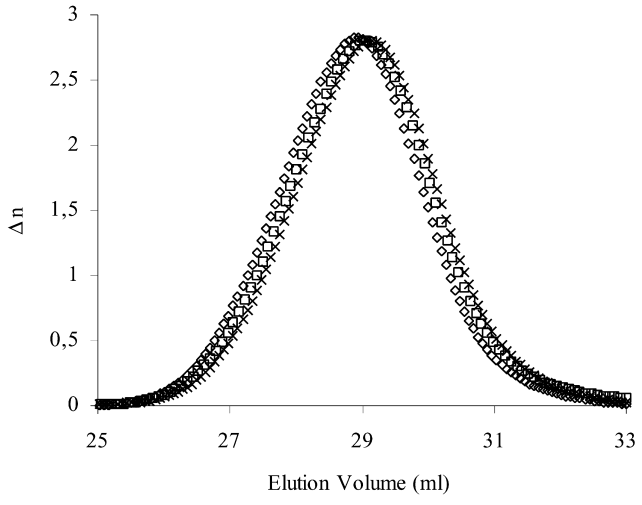


Fig. 3. SEC chromatograms (refractometric detection) of dextran at different steps of the silylation process: (◇) initial dextran; (□) dextran dried under reduced pressure at 100 °C for one night; (×) dextran recovered after the steps of the silylation process except addition of HDMS (see Section 2).

In the present case, HMDS was used for silylation, preferably to TMSCl whose reaction leads to HCl which could degrade dextran chains. The silylation mechanism with HMDS is shown in Scheme 2. Hydroxyl functions react with HMDS, to give silylated dextran and Me_3SiNH_2, which then reacts with a dextran OH group yielding NH_3 as a byproduct. Whatever the conditions used for the silylation reaction with HMDS, no degradation of dextran chain was evidenced by SEC-MALLS as typically shown in Fig. 3.

Influence of many parameters on silylation yields was investigated: medium temperature, reaction time, amount of silylating agent, addition of a solvent of the silylated dextrans and of a catalyst. Results are discussed hereafter.

3.2. Influence of reaction time and medium temperature

Firstly a silylation experiment was carried out with D^{I}_{40} at 50 °C with 2 mol HMDS per mol OH, and in DMSO in which the dextran samples were readily soluble. This reaction began in homogeneous medium but as silylation proceeded, partially silylated dextran got insoluble and reaction went on under heterogeneous conditions. Progress of the protection reaction was followed by running parallel experiments stopped after various given reaction times (Fig. 4).

Concerning the effect of temperature, it was observed that for a given batch of dextran (here D^{I}_{40}), the silylation yield reached a maximum that depended this parameter. The fastest silylation reaction and the highest protection yield (95%) were obtained at 80 °C.

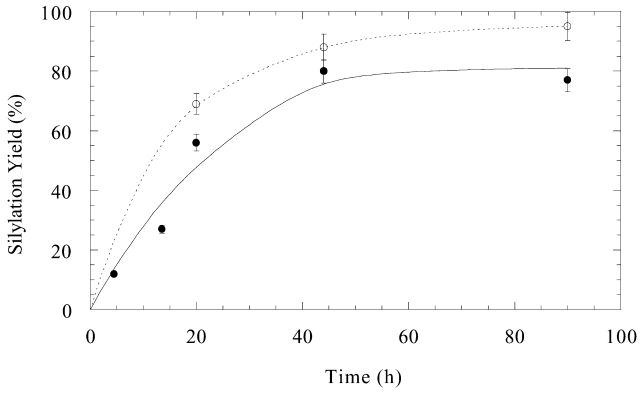


Fig. 4. Kinetics of silylation. Reactions were carried out in DMSO with 2 mol HDMS per mol OH ((●) D^1_{40} at 50 °C; (○) D^1_{40} at 80 °C). Silylation yields were calculated from Eq. (1) or Eq. (2).

3.3. Influence of silylation reagent concentration and composition

The effect of HMDS concentration on the silylation yields was investigated and the results are shown in Table 1. An increase in HMDS/OH molar ratio enhanced the yield of protection. However, whatever the batch of dextran T40 used, after a 20 h reaction at 50 °C, the protection yield remained rather low (<78%) even in the presence of a large excess of HMDS (HMDS/OH molar ratio = 5). This result was explained by the fact that, as silylation proceeded, the reaction medium became more and more heterogeneous.

As pointed out earlier, silylation reactions can also be carried out with HMDS in the presence of TMSCl [20]. In fact, when few percents of TMSCl were added to HMDS, a significant activation effect was noticed. HCl formed by the reaction of an OH function with TMSCl is trapped by NH_3 in situ formed by the alcoholysis of HMDS. As shown in Table 2, the silylation yield significantly increased when 10% TMSCl were added to HMDS. For one of the dextran batches this yield even reached 100%, proving a complete protection of the OH functions. On the other hand, tertiary amines are well-known for activating the silylation reaction as well [24]. As shown in Table 2, addition of 10% NEt_3 (previously dried over BaO) increased the silylation yield from 56 to 79%.

Table 1
Dependence of silylation yield and DS on HMDS/OH ratio. Each silylation was carried out in DMSO at 50 °C for 20 h

Initial dextran	HMDS/OH molar ratio	Silylation yield (%)[a]	DS[b]
D^1_{40}	2.00	56	1.7
	3.00	70	2.1
	4.00	73	2.2
D^2_{40}	0.25	37	1.1
	0.50	68	2.0
	2.00	76	2.3
	5.00	78	2.3

[a] Calculated from Eq. (1).
[b] Calculated from Eq. (3).

Table 2
Effect of addition of TMSCl or NEt_3 on the silylation yield and DS. Each silylation was carried out in DMSO at 50 °C for 20 h using 2 mol silylating agent per mol OH

Initial dextran	Silylating agent	Silylation yield (%)[a]	DS[b]
D^1_{40}	HMDS	56	1.7
	HMDS + 10% NEt_3[c]	79	2.4
	HMDS + 10% TMSCl[c]	67	2.0
D^2_{40}	HMDS	76	2.3
	HMDS + 10% TMSCl[c]	100	3.0

[a] Calculated from Eq. (1).
[b] Calculated from Eq. (3).
[c] In mol% (% with respect to HDMS mol).

3.4. Addition of a solvent of silylated dextrans

In the first sets of experiments, the silylation reactions were carried out in DMSO in which dextran is perfectly soluble but not the silylated derivatives. Addition of a solvent of the partially silylated dextran after its effective precipitation from DMSO, typically after ca. 4 h, was then experienced in order to make the reaction homogeneous. Two solvents, THF or toluene, were then added to DMSO in various amounts (Table 3). The silylation reactions were carried out at 50 °C for 20 h with 2 mol HMDS per mol OH either directly in the presence of the co-solvent or according to the following procedure: first the reaction started in pure DMSO, then after precipitation of silylated dextran (i.e. after about 4 h), the second solvent was added.

When the co-solvent is added after precipitation of partially silylated dextran, silylation yield increased from 56 to 70% for THF and from 56 to 88% for toluene after 20 h (DMSO/co-solvent: 1/1 v/v) (Table 3). No significant effect of the DMSO/THF ratio on the protection yields was noticed.

Table 3
Effect of co-solvent on silylation yield and DS. Initial dextran = D^1_{40}. Each silylation was carried out with 2 mol HMDS per mol OH at 50 °C for 20 h

Solvent mixture (v/v)	Silylation yield (%)[a]	DS[b]
DMSO	56	1.7
DMSO/THF (1/1)[c]	52	1.6
DMSO/THF (1/1)[d]	70	2.1
DMSO/THF (4/1)[d]	72	2.2
DMSO/toluene (1/1)[c]	83	2.5
DMSO/toluene (1/1)[d]	88	2.6

[a] Calculated from Eq. (1).
[b] Calculated from Eq. (3).
[c] Co-solvent added at the beginning of the silylation reaction.
[d] Co-solvent added after precipitation of partially silylated dextran in DMSO.

When the silylation experiments were carried out directly in the presence of the co-solvent, the protection yields observed were lower than those obtained in the two-step reaction.

In conclusion, use of toluene as co-solvent instead of THF proved to be more efficient in terms of silylation yield.

3.5. Influence of the dextran batch

Changes in silylation yields with medium temperature and reaction time, shown in Tables 1 and 2 and in Fig. 5 also depend on the batch of dextran (D^1_{40} and D^2_{40}). Thus, when silylation reactions were carried out in DMSO at 50 °C for 20 h with 2 mol HMDS per mol OH, the protection yield increased from 56% (D^1_{40}) to 76% (D^2_{40}). The addition of 10% TMSCl led to the complete silylation of D^2_{40}, while only 67% yield was obtained under the same conditions with D^1_{40} (Table 2).

The results of silylation show that, whatever the conditions, D^1_{40} was less reactive than D^2_{40}. These different reactivities between two batches of dextran with similar $\overline{M_n}$ and $\overline{M_w}$ are likely due to different branching ratios. If one assumes that an increase in branching ratio provokes a decrease in the accessibility of OH functions towards silylation, then it should be concluded that D^1_{40} is more branched than D^2_{40}. This assumption has not been verified yet.

3.6. Totally silylated dextrans

As previously reported by some of us [12], complete silylation of D_{10} was achieved by using 4 mol HMDS, 0.2 mol NEt_3 at 80 °C for 90 h in a final DMSO/THF (6/4 v/v) solvent mixture. Despite its higher molecular weight, complete silylation of D^2_{40} could be also obtained by using either 2 mol HMDS + 10% TMSCl at 50 °C for 20 h in DMSO (Table 2) or 4 mol HMDS, 0.2 mol NEt_3 at 60 °C for 48 h in a final DMSO/THF (6/4 v/v) solvent mixture. The quantitative silylation of dextran can be further evidenced by FT-IR spectroscopy which displays the complete disappearance of the hydroxyl absorption band at ca. 3500 cm^{-1} [12]. Six new absorptions related to the trimethylsilyl group [20] can be detected at 750, 842, 874, 1020, 1156, 1250 cm^{-1}.

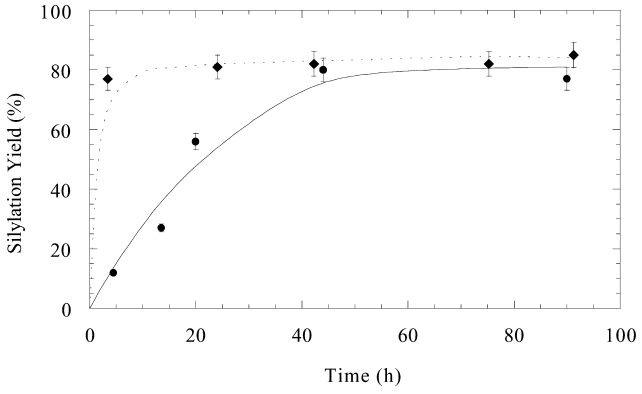


Fig. 5. Kinetics of silylation. Reactions were carried out in DMSO at 50 °C with 2 mol HDMS per mol OH ((●) D^1_{40}; (◆) D^2_{40}). Silylation yields were calculated from Eq. (1) or Eq. (2).

3.7. Thermal properties of (partially) silylated dextrans

Partially and totally silylated dextrans recovered by precipitation in cooled water and complete drying under intensive vacuum were characterized by temperature-modulated DSC (see Section 2). T_g values of the silylated dextrans are mainly comprised between 120 and 140 °C whatever the dextran batch and the silylation degree, at least above a silylation yield of 55%. Interestingly enough, during the course of our experiments it was observed however that residual DMSO could substantially decrease the T_g values of the (partially) silylated dextran. As a typical example, Fig. 6 shows the effect of increasing amounts of DMSO on the T_g values of a fully silylated dextran (D^2_{40}). In these experiments molar fraction of absorbed DMSO (F_{DMSO}) was calculated from the ^1H NMR spectra by Eq. (4)

$$F_{DMSO} = \frac{(A_{DMSO}/6)}{(A_{DMSO}/6 + A_{anomeric\ H})} \quad (4)$$

where A_{DMSO} was the relative area of DMSO protons at 2.6 ppm (solvent: $CDCl_3$).

These results highlight the necessity of a complete removal of this solvent for accurate T_g measurements. This observation is of great interest since it has been previously reported by some of us [12] that for a given dextran molecular weight, increasing the degree of silylation seemed to enhance the T_g values. Actually, the present study highlights the effect of residual DMSO as an efficient plasticizer for partially and totally silylated dextrans. The plasticizing effect of DMSO could be more pronounced at lower silylating degree as a result of more specific interactions between this polar solvent and the remaining OH

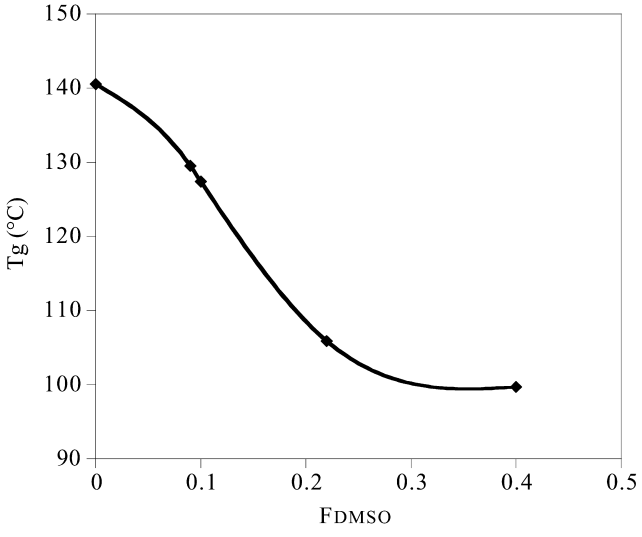


Fig. 6. Influence of DMSO on T_g of the fully silylated dextran (D^2_{40}). F_{DMSO} was calculated from Eq. (4).

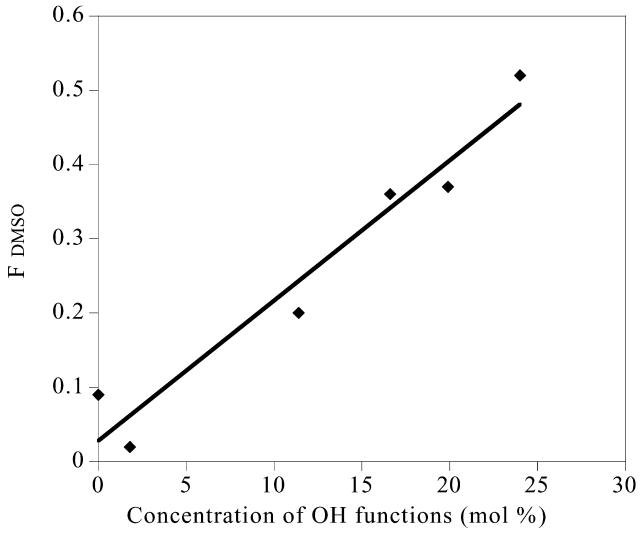


Fig. 7. Relation between the molar fraction of DMSO absorbed in partially silylated dextran (F_{DMSO}) and the content of free OH remaining in the polymer. (D_{10}, polymer dried at 50 °C under vacuum for 20 h, % with respect to initial OH functions).

functions. In fact, it was shown that even after a given drying stage at 50 °C under vacuum (10^{-2} mmHg) for 20 h, the residual DMSO concentration absorbed in silylated dextrans was directly proportional to the remaining free hydroxyl content. This is nicely illustrated by Fig. 7 where it is seen that F_{DMSO} increases linearly with the content of OH functions spread along the dextran chains. As a direct result, a dextran chain characterized by a lower silylation degree will display a lower T_g value due to the plasticizing effect of the increased content in residual DMSO.

3.8. Synthesis of polyester-grafted dextrans

Some polyester-grafted dextrans, namely (PCL-grafted dextran) [12] and polylactide-grafted dextran (PLA-grafted dextran) (results not published), were synthesized according to the strategy shown in Scheme 1.

The second step of this synthetic scheme relies on the ROP of CL or LA in toluene solution by initiation with the remaining free hydroxyl groups of partially silylated dextrans. These –OH functions were previously activated by a catalytic amount of either aluminum triisopropoxide ($Al(O^iPr)_3$), triethylaluminum ($AlEt_3$) or stannous octoate ($Sn(Oct)_2$) (Table 4). First it is worth noting that the resulting grafted copolymers are characterized by higher molecular weight (relative to PS calibration in SEC) than the starting partially silylated dextran multifunctional macroinitiator. Furthermore the molecular weight distributions of the grafted copolymers are symmetrical with a polydispersity index ranging between 1.4 and 1.6. These observations attest for the efficiency of the polymerization reaction i.e. of the polyester chain grafting along the polysaccharide backbone.

The polyester weight fraction in the copolymers (F_{PCL} or F_{PLA}) was determined by either gravimetry after precipitation of the reaction product from heptane or ^{1}H NMR spectroscopy. F_{PCL} (F_{PLA}) was calculated by ^{1}H NMR by comparison of the relative areas of the '–CH_2–O(CO)' methylene protons at 4.1 ppm (of the '–(CO)–CH–O–' methine protons located at ca. 5.2 ppm) with the glucosidic methine and methylene protons in the range 3.0–4.0 ppm. In case of PCL-grafted dextrans, ^{1}H NMR spectroscopy in $CDCl_3$ led to F_{PCL} values which could exceed the initial feed weight fraction of ε-caprolactone f_{CL} and were higher than the gravimetric ones. These results were interpreted by the formation of a stable core-shell cylindrical conformation as a result of the presence of PCL grafts spread along the silylated dextran backbone [12]. Interestingly enough this behavior was not observed in case of PLA-grafted dextrans for which F_{PLA} were in good agreement with f_{LA} values at least within the range of compositions and molecular weights herewith investigated. More detailed data will be provided in a forthcoming paper.

The third step consists of the removal of the trimethylsilyl

Table 4
Characteristics of polyester-grafted silylated dextran obtained by ROP in toluene (entries 1–3: M = ε-caprolactone, 60 °C, 68 h, ([Activator]/[OH] = 0.05); entry 4: M = ε-caprolactone, 100 °C, 44 h, ([Activator]/[OH] = 0.05); entries 5 and 6: M = D,L lactide, 100 °C, 20 h, ([Activator]/[OH] = 0.03)

Sample	Silylated dextran		$[M]_0/[OH]$	Activator	f_M[a]	F_M[b]		Conversion[c] (%)	$\overline{M_n}$[d]	$\overline{M_w}/\overline{M_n}$
	Initial dextran	DS				Grav	^{1}H NMR			
1	D_{10}	2.8	20	$AlEt_3$	0.64	0.41	0.94	67	34,700	1.4
2		2.6	20	$Al(O^iPr)_3$	0.77	0.73	0.95	88	31,300	1.4
3		2.8	20	$Sn(Oct)_2$	0.64	0.50	0.84	83	36,500	1.5
4	D^2_{40}	2.7	5	$Sn(Oct)_2$	0.32	0.26	0.39	100	34,300	1.6
5		2.7	5	$Sn(Oct)_2$	0.21	ND	0.20	95	ND	ND
6		2.6	12	$Sn(Oct)_2$	0.48	ND	0.51	93	37,000	1.8

[a] f_M = initial feed weight fraction of the cyclic ester monomer.
[b] F_M = polyester weight fraction in the copolymers, determined by either gravimetry or ^{1}H NMR spectroscopy (see text).
[c] Conversion with respect to the initial cyclic ester monomer.
[d] Number-average molecular weight as determined by SEC in reference to a polystyrene calibration.

protecting groups by treatment of the graft copolymers in THF solution (10 wt%) with a slight excess of an aqueous HCl solution (1 M) with respect to the number of '$-OSiMe_3$' functions. Complete deprotection was proved by FT-IR spectroscopy by the disappearance of absorption bands of trimethylsilyl functions in favor of a large absorption at ca. 3500 cm^{-1} typical of hydroxyl groups. It is important to mention that separate experiments carried out on dextran and PCL (or PLA) homopolymers under the aforementioned deprotection conditions attested for the total absence of side degradation reactions as evidenced by SEC analysis.

4. Conclusion

The silylation reaction of dextran by means of HMDS was carried out in DMSO in which dextran is readily soluble. Silylation thus starts under homogeneous conditions and further proceeds heterogeneously as partially silylated dextrans get insoluble in DMSO. The influence of various parameters on the extent of silylation was studied. First it was found that silylation yield increases with reaction time, temperature and with the HMDS/OH initial ratio. Another important parameter is the initial dextran form and related branching.

However, whatever the reaction conditions, the silylation yield was systematically smaller than 80%. This limitation was attributed to the precipitation of silylated dextran in the course of reaction. Addition of either a solvent of this silylated dextran (THF or toluene) or of an activator such as NEt_3 or TMSCl led to a significant increase in the protection yield. Finally it was shown that under given conditions, totally silylated dextran could be recovered.

As far as the thermal properties of (partially) silylated dextran are concerned, the role of residual DMSO in the material was found to be very important, as the T_g value decreased with the increase in DMSO concentration. Moreover, it was shown that the residual DMSO concentration depended on the silylation yield, more likely as a result of hydrogen bonds between the OH groups and this solvent.

The silylation step of dextran is the first reaction of the three-step controlled synthesis of biodegradable polyester-grafted dextran amphiphilic copolymers. The detailed synthesis and the complete characterization of these new amphiphilic macromolecules will be published in the near future.

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