



**HAL**  
open science

# Silylation Reaction of Dextran: Effect of Experimental Conditions on Silylation Yield, Regioselectivity, and Chemical Stability of Silylated Dextrans

Cécile Nouvel, Philippe Dubois, Edith Dellacherie, Jean-Luc Six

► **To cite this version:**

Cécile Nouvel, Philippe Dubois, Edith Dellacherie, Jean-Luc Six. Silylation Reaction of Dextran: Effect of Experimental Conditions on Silylation Yield, Regioselectivity, and Chemical Stability of Silylated Dextrans. *Biomacromolecules*, American Chemical Society, 2003, 4 (5), pp.1443-1450. 10.1021/bm034119m . hal-02945692

**HAL Id: hal-02945692**

**<https://hal.univ-lorraine.fr/hal-02945692>**

Submitted on 22 Jan 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Silylation reaction of dextran: effect of experimental conditions on silylation yield, regioselectivity and chemical stability of silylated dextrans

*Cécile Nouvel<sup>1</sup>, Philippe Dubois<sup>2</sup>, Edith Dellacherie<sup>1</sup>, Jean-Luc Six<sup>1\*</sup>*

<sup>1</sup>Laboratoire de Chimie-Physique Macromoléculaire (LCPM), UMR CNRS-INPL 7568,  
Groupe ENSIC, 1 rue Grandville, B.P. 451, 54001 Nancy cedex, FRANCE.

<sup>2</sup>Laboratory of Polymeric and Composite Materials (LPCM), University of Mons-Hainaut,  
Place du Parc 20, B-7000 Mons, BELGIUM.

Email : [Jean-Luc.Six@ensic.inpl-nancy.fr](mailto:Jean-Luc.Six@ensic.inpl-nancy.fr)

Fax : 33(0)3-83-37-99-77 ; Tel : 33(0)3-83-37-52-61

\*corresponding author

(submitted to Biomacromolecules)

ABSTRACT : The controlled synthesis of biodegradable copolymers of dextran grafted with aliphatic polyesters, firstly requires to prepare polysaccharide derivatives soluble in organic solvents. Silylation of dextran can thus lead to such organosoluble derivatives and allows the polymerization of cyclic esters initiated from the non-silylated OH functions. Silylation of dextran was studied in DMSO by different reactants such as 1,1,1,3,3,3-hexamethyldisilazane (HMDS) in the presence of various catalysts and N,O-bis(trimethylsilyl)acetamide (BSA). According to the silylating agent and the used experimental conditions, it was possible to obtain highly or totally silylated dextrans. In parallel, an investigation of the chemical stability of the dextran chain during silylation was performed. Thus it was found that, when used at 50°C, HMDS with or without catalysts gives a relatively high silylation yield and does not alter the dextran chain length, while at 80°C, dextran degradation was observed. BSA is a very good silylating agent, which allows reaching 100 % silylation even at 50°C but provokes the degradation of the polysaccharide chains. The work was completed by a study of the reactivity order of the glucosidic OH functions towards silylation reaction. This order was found to be (OH<sup>2</sup>>OH<sup>4</sup>>OH<sup>3</sup>) as already reported for other reactions. 2D-NMR of highly silylated dextrans demonstrated that they are constituted of both quantitatively silylated glucose units and two types of disilylated ones.

KEYWORDS : dextran, HMDS, BSA, polyester-grafted dextran, amphiphilic copolymers, 2D-NMR

## 1) Introduction

Since the last century [1], silylation of polysaccharides has attracted much attention. A lot of research was carried out in order to increase either thermal stability of these polymers at high temperature, which is required in the industrial processes [2], or their solubility in organic solvents [3].

The first silylations were performed under heterogeneous conditions in pyridine [1,4] or formamide [5] because of the insolubility of usual polysaccharides. Afterwards, Keilich *et al.* [6] improved the experimental conditions adding drop by drop an ether solution of silylating agent on polysaccharide. In this case, silylation began in heterogeneous medium but as modification proceeded, partially silylated polysaccharide got soluble in ether phase.

Silylating agents generally used are 1,1,1,3,3,3-hexamethyldisilazane (HMDS) or chlorotrimethylsilane (TMSCl) respectively generating  $\text{NH}_3$  and  $\text{HCl}$ , or a mixture of both. Use of TMSCl requires a base to neutralize the generated  $\text{HCl}$  and pyridine is usually used for this purpose.

Complete silylation of linear polysaccharides like amylose, pullulan or cellulose [6 - 10] were reported. But, to the best of our knowledge, complete silylation of lowly branched polysaccharides like dextran has not been reported until recently.

Recently, we reported [11] on the partial or quantitative silylation of dextran. This dextran (Figure 1) consists of  $\alpha$ -D-glucose units having preponderant  $\alpha$  (1 $\rightarrow$ 6) glucosidic linkages while few percents of (1 $\rightarrow$ 3) glucosidic linkages provide side chains. The silylation of dextran chains with HMDS was the first step of the controlled synthesis of new amphiphilic polyester-grafted dextrans [11, 12] depicted in Scheme 1. This synthesis, which permits the combination of biodegradable hydrophobic polyesters with biodegradable hydrophilic dextran, leads to totally biodegradable amphiphilic grafted copolymers. These products could be useful as environmentally friendly surfactants, or in formulation of drug delivery systems.

In our previous paper [11] influence of parameters such as molar mass of initial dextran, temperature medium and reaction time, HMDS/OH ratio, addition of a solvent of partial silylated dextran (co-solvent) on silylation yield was described.

In this paper we firstly report the influence of several catalysts for the silylation reaction with HMDS and the use of another silylating reagent, i.e. N,O-bis(trimethylsilyl)acetamide (BSA) on the dextran silylation yields. The second part of this paper is devoted to the study of the reactivity order of each dextran alcohol function towards silylation. In the last part of the paper, we investigate the stability of polysaccharide chains all along the silylation process.

## **2) Materials and methods**

### **2.1) Materials**

Dextran T40 ( $\overline{M}_n = 29\ 000\ \text{g mol}^{-1}$ ,  $I = 1.3$ ) was purchased from Pharmacia Biotech and dried under a reduced pressure at 100°C for one night. No degradation of the polysaccharide chains was evidenced under these drying conditions as attested by size exclusion chromatography coupled to a multi-angle laser light scattering detector (SEC-MALLS). 1,1,1,3,3,3-hexamethyldisilazane (HMDS) (99.9%), chlorotrimethylsilane (TMSCl) (99%), N,O-bis(trimethylsilyl)acetamide (BSA), hexamethylphosphoric triamide (HMPA) (99%), N-methylimidazole (NMI) (99%), saccharin (99%), tetrabutylammonium fluoride (TBAF) (1M solution in tetrahydrofuran) were purchased from Aldrich and were used without any further purification.

Toluene and dimethylsulfoxide (DMSO) were refluxed and distilled over  $\text{CaH}_2$ , then stored under nitrogen atmosphere. Just before use, these solvents were respectively dried over  $\text{CaH}_2$  or polystyryl lithium and distilled again.

## 2.2) Dextran silylation

Silylation was carried out in DMSO in a previously dried and nitrogen purged two-necked round bottom flask equipped with a stopcock. Once 1 g of dried dextran was totally dissolved in 30 ml of DMSO, desired amounts of silylating agent and catalyst (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. The medium was concentrated and the expected silylated dextran was recovered by precipitation from cooled water (no hydrolysis of the  $-\text{OSiMe}_3$  groups was evidenced during this precipitation step).

## 2.3) Silylation yields

### 2.3.1) Direct method

Protection yields were calculated by  $^1\text{H}$  NMR in  $\text{CDCl}_3$  (Figure 2a) or in  $\text{d}_6\text{-DMSO}$  depending on the extent of silylation, using Eq. (1) where  $A_{\text{OSiMe}_3}$ ,  $A_{\text{anomeric H}}$  are the respective areas of the trimethylsilyl group (at 0.15 ppm in  $\text{CDCl}_3$  or 0.18 ppm in  $\text{d}_6\text{-DMSO}$ ) and of the anomeric proton centered at 4.7 ppm in  $\text{CDCl}_3$  or  $\text{d}_6\text{-DMSO}$ . Details of this direct method are given in our previous paper [11]. Highly silylated dextrans (silylation yield > 50%) were soluble in  $\text{CDCl}_3$  while slightly silylated dextrans were soluble in  $\text{d}_6\text{-DMSO}$ .

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

### 2.3.1) Indirect method

Confirmation of the protection yields was obtained after reaction between the free remaining OH functions of partially silylated dextrans with an excess of trichloroacetylisocyanate [13] (Scheme 2). Thus, silylation yields could be calculated from

the spectrum shown in Figure 2b using either Eq. (2) or (3), where  $(A'_{\text{anomericH}} + A'_{\text{glucosidicH}})$  and  $A_{\text{NH}}$  are the respective areas of the multiplets between 3 and 5.5 ppm and corresponding to the urethane protons [8.5 - 9.5 ppm].

$$\text{Silylation yield (\%)} = 100 - \frac{A_{\text{NH}}}{A'_{\text{anomericH}} + A'_{\text{glucosidicH}}} \times \frac{7 \times 100}{3} \quad (2)$$

$$\text{Silylation yield (\%)} = \frac{A_{\text{OSiMe}_3}}{A'_{\text{anomericH}} + A'_{\text{glucosidicH}}} \times \frac{7 \times 100}{27} \quad (3)$$

Similar silylation yields were obtained regardless of equations (1), (2) or (3).

#### 2.4) Deprotection of the silylated dextran

Silylated dextrans were dissolved in THF and 0.02 equivalent of HCl (aqueous solution - 0.1M) with respect to the number of “-O-SiMe<sub>3</sub>” groups was then added. After 2 h at room temperature, the products were recovered by precipitation in ethanol, filtration and drying under vacuum.

#### 2.5) Characterization techniques

<sup>1</sup>H-NMR spectra were recorded using a Bruker Avance 300 apparatus in d<sub>6</sub>-DMSO, CDCl<sub>3</sub> or D<sub>2</sub>O. Size exclusion chromatography (SEC) of dextrans was performed at room temperature using a Waters HPLC pump (Waters 410) equipped with a DG-1310 degasser, 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 MALLS and differential refractometry (Waters 410). A refractive index increment of 0.146 was used. Dextrans solutions (10 mg/ml) were prepared by dissolution in the aqueous eluent (0.1 M NaNO<sub>3</sub>, 6.15

$10^{-3}$  M  $\text{NaN}_3$ ) and were left under vigorous stirring for 24 h. Filtration of these solutions (Millex GSWP 0.22  $\mu\text{m}$ ) was carried out right before injection.

HMQC (Heteronuclear Multiple Quantum Coherence) and Cosy  $45^\circ$  (Proton Correlation Spectroscopy) were run on 300MHz Bruker spectrometer (Bruker SA). 32 transients were acquired of respectively 256 complex points in t1 (1024 in t2) and 128 complex points in t1 (2048 in t2). Prior to Fourier transform, zero filling on t1 dimension was performed until 512 points and both dimensions were multiplied by cosine and sine functions for HMQC and COSY experiments respectively.

### **3) Results and discussion**

#### **3.1) Silylation of dextran chains**

##### **3.1.1) Silylation with HMDS**

In our previous paper [11], silylation of dextran with HMDS was carried out in DMSO. Under these conditions hydroxyl functions react with HMDS to give silylated dextran and  $\text{Me}_3\text{SiNH}_2$ , which then reacts with free alcohol groups yielding  $\text{NH}_3$  as by product. Silylation starts under homogeneous conditions and further proceeds heterogeneously as partially silylated dextrans get insoluble in DMSO. The influence of various parameters, such as dextran molar mass, medium temperature, reaction time, HMDS/OH ratio, and addition of a co-solvent was investigated. Silylation yields were calculated using either direct or indirect methods. The indirect method requires a reaction between the free remaining OH functions of partially silylated dextrans with an excess of trichloroacetylisocyanate. This isocyanate is known to react almost instantaneously with water, primary or secondary hydroxyl groups and requires only 2-3 min to react with tertiary alcohols or phenols. If some water reacts in the same time with the isocyanate, trichloroacetamide is formed and is characterized by two singlets at 6.7 and 6.2 ppm in  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) (Figure 2b). The reaction of dextran OH

functions with trichloroacetylisocyanate gives a multiplet [4.5 – 5.5 ppm], which corresponds not only to the anomeric protons but also to the glucosidic protons carried by carbons bearing urethane functions. The multiplet [3 – 4.5 ppm] corresponds to the glucosidic protons carried by carbons bearing -OSiMe<sub>3</sub> groups (Figure 2). Similar silylation yields were obtained by both methods.

It was found that silylation yield increases with reaction time, temperature, HMDS/OH initial ratio and decreases with dextran molar mass. 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 a solvent of the silylated dextran (THF or toluene) led to a significant increase in the protection yield.

In this work, whose results are described here, we studied the influence of the addition to HMDS of different catalysts such as chlorotrimethylsilane (TMSCl) or nucleophilic compounds like hexamethylphosphoric triamide (HMPA), N-methylimidazole (NMI), saccharin or tetrabutylammonium fluoride (TBAF) on the silylation yields. Acidic catalysts like HCl, p-toluenesulfonic acid or trifluoroacetic acid are known to increase the HMDS reactivity and thus the silylation yield. But in our study, these acidic agents were excluded because of their potential degrading action over the dextran chains.

As shown in Figure 3, silylation yield increases with the amount of TMSCl in the HMDS/TMSCl silylating mixture. Thus, quantitative silylation was observed when 2 mol of silylating mixture composed of 1.8 mol of HMDS + 0.2 mol of TMSCl per mol OH function were used. Explanation of these results is given by Nagy [14]. TMSCl, which is known to be more reactive than HMDS, first reacts with the hydroxyl functions leading to HCl as by-product. HCl is then captured by HMDS to product NH<sub>3</sub> and new TMSCl (Scheme 3).

In case of nucleophilic catalysts, four reagents were tested (HMPA, NMI, saccharin or TBAF) and their influence on dextran silylation yields are shown in Table 1. All the catalysts, except NMI, lead to an increase in the silylation yield in comparison with the experiment carried out without activator, but the best one proved to be saccharin. The activation of HMDS by these nucleophilic products is explained by the formation of pentacoordinated intermediate species [15]. These species are obtained by the rapid reaction between catalyst and HMDS and exhibit a higher reactivity than HMDS does towards hydroxyl functions.

In conclusion, when silylation is carried out with HMDS, silylation yields could be controlled by adding different catalysts. It was shown that quantitative silylation of dextran chains could be achieved by an adequate selection of the experimental conditions.

### **3.1.2) Silylation with BSA**

Another silylating reagent was also investigated. N,O-Bis(trimethylsilyl)acetamide (BSA) was chosen because of its high reactivity towards alcohol functions and because it does not react with DMSO, unlike its trifluoro homologous [16]. BSA exists under two tautomeric forms but the imidate form is preponderant [17]. Dextran hydroxyl functions react with the –OSiMe<sub>3</sub> group of BSA to produce silylated dextran and N-trimethylsilyl acetamide as by-product (Scheme 4). This by-product is in equilibrium with its O-tautomeric form, which can react a second time with alcohol functions providing silylated dextran and acetamide. Experiments were carried out with various molar BSA / OH ratios.

As shown in Figure 4, BSA presents some advantages. First, increasing the BSA / OH molar ratio enhances the silylation yield as already observed with HMDS [11]. But with similar silylating reagent amount, BSA leads to higher silylation yields than HMDS does, even if HMDS is activated with catalysts. Thus, a fully silylated dextran could be obtained using 2 mol BSA per mol OH. Finally, BSA also enhanced the silylation kinetics: when

HMDS was used, partially silylated dextrans got insoluble in DMSO after about 4 h; but with BSA this precipitation was observed before 1 h, which means that highly silylated dextrans were obtained more rapidly in the latter case. Temperature of the reaction medium had no influence on the silylation yield when 1 mol BSA per mol OH was used as 90 % silylation was observed whatever the temperature (50°C or 80°C). In addition, using adequate experimental conditions (BSA and a co-solvent (toluene)) led to quantitative silylation of the dextran hydroxyl functions (Figure 4). It is worth reminding that only 83% silylation yields was obtained with HMDS when DMSO / toluene mixture (2/1 v/v) was used as initial reaction medium and 88% when toluene was added after precipitation of partially silylated dextran in DMSO medium [11].

In conclusion, BSA is a silylating agent more reactive towards polysaccharide hydroxyl groups than HMDS and allows complete silylation of dextran, even at 50°C.

### **3.2) Alcohol reactivity order towards silylation**

In order to evaluate the reactivity of each alcohol function carried by dextran chains, a precise attribution of the NMR dextran resonance signals ( $^1\text{H}$  and  $^{13}\text{C}$  – DMSO- $d_6$ ) was achieved using 2D-NMR (Cosy 45° and HMQC). The results obtained are in agreement with published results [18].

Generally in polysaccharides, each hydroxyl group has a specific reactivity [19] due to steric and electronic effects. In case of dextran, reactivity of OH functions has often been studied towards acetylation [20]. No information about the reactivity of OH functions towards silylation can be found.

Assuming that each glucose unit exhibits the same accessibility and overlooking the reactivity changes with the substitution of one OH function, the study of  $^1\text{H}$  NMR spectra of slightly silylated dextrans characterized by different silylation yields (< 40%) allows to

determine the OH functions to be firstly silylated. As shown in Figure 5, the chemical shift of each OH function increases with the increasing silylation yield, while the shape of the glucosidic proton multiplet is strongly modified. The doublet corresponding to the OH carried by the carbon atom C<sup>2</sup> (Figure 2), which is noted in the following text OH<sup>2</sup> is rapidly vanishing when the protection yield increases. Thus, OH<sup>2</sup> seems to be the most reactive function towards silylation. This high reactivity is related to its high basicity due to its hydrogen bonding with the O carried by carbon atom C<sup>1</sup>. Further comparing the partially silylated dextrans at different silylation yield, it also comes out that OH<sup>4</sup> is more reactive than OH<sup>3</sup>. The (OH<sup>2</sup> > OH<sup>4</sup> > OH<sup>3</sup>) reactivity order observed in our case is in agreement with those generally accepted in acetylation reaction [20]. Figure 6, which gives the HMQC spectrum of a 95% silylated dextran confirms the presence of quantitative silylated glucose units (noted GU234) but also two types of disilylated ones: silylated on positions 2 and 3 (GU23) and on positions 2 and 4 (GU24). We have to mention here that the assignment of each peak in the Figure 7 is only valid for a 95 % silylated dextran as partial protection can lead to unpredictable effects in the chemicals shifts of the protons and carbons of the glucose units [20]. The observation here before mentioned allows us to conclude that highly silylated dextrans exhibit both unprotected OH<sup>4</sup> and OH<sup>3</sup>, with a preponderance for the last one.

### **3.3 ) Stability of dextran chain during silylation process**

The stability of dextran chains during the silylation process was also investigated. Thus, several partially silylated dextrans obtained under various experimental conditions were deprotected under very mild conditions, using a catalytic amount of HCl with respect to the number of “-O-SiMe<sub>3</sub>” groups. Previously, no degradation of dextran chains was evidenced under these conditions. The silylated dextrans were then deprotected and the resulting compounds (noted HSD) were analyzed by aqueous SEC. Their SEC chromatograms were

then compared to that of initial dextran in order to verify the dextran stability during the silylation process.

Whatever the experimental conditions (long reaction time, presence of co-solvent or catalyst), no dextran degradation was observed when silylation was carried out with HMDS at 50°C as shown in Figure 7. Thus, samples noted HSD2, 3, 4 display aqueous SEC chromatograms similar to that of initial dextran. In contrast, when HMDS was used at 80°C, dextran length decreased. Thus, silylation of dextran with HMDS proceeds without degradation only when temperature medium is not too high.

On the contrary and whatever the experimental conditions, degradation of dextran chains was always observed when silylation was carried out with BSA (Table 2). Thus, when 1 mol BSA per mol OH functions was used, the length of dextran chains undergoes a significant decrease, independently of the studied reaction temperature. Moreover, the presence of a co-solvent or increasing the BSA / OH molar ratio, which proved to be necessary conditions to obtain high silylation yields, increase the extent of dextran chain degradation as well.

#### **4) Conclusion**

Silylation of dextran chains was carried out under various experimental conditions. High protection yields could be observed using HMDS as silylating reagent. In this case, the use of catalysts or co-solvent favors the increase in the silylation yields and leads to complete silylation under specific conditions (1.8 mol HMDS added with 0.2 mol TMSCl per mol OH function). HMDS is a mild silylating reagent when used at 50°C, but degradation of the dextran chains was observed when the reaction was carried out at 80°C.

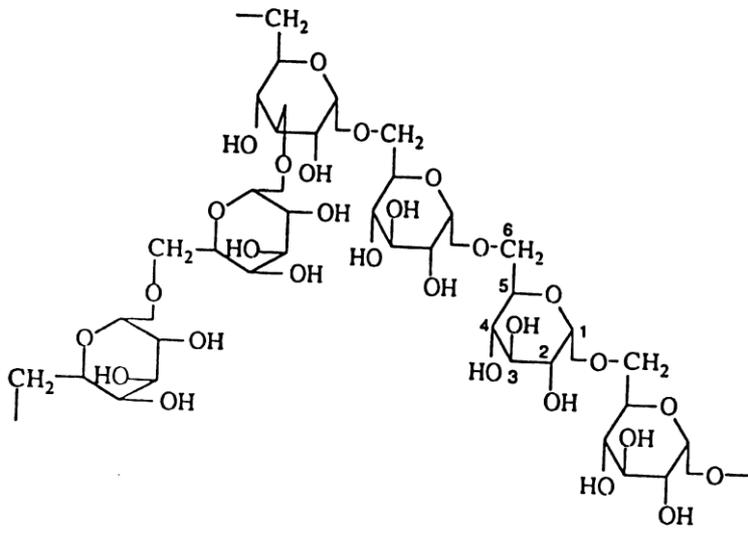
Silylation with another reagent, N,O-Bis(trimethylsilyl)acetamide (BSA), was also experimented. BSA is more reactive than HMDS and leads faster to high and even

quantitative protection yields. Unfortunately, this reagent triggers a significant reduction of the polysaccharide chain length whatever the experimental conditions.

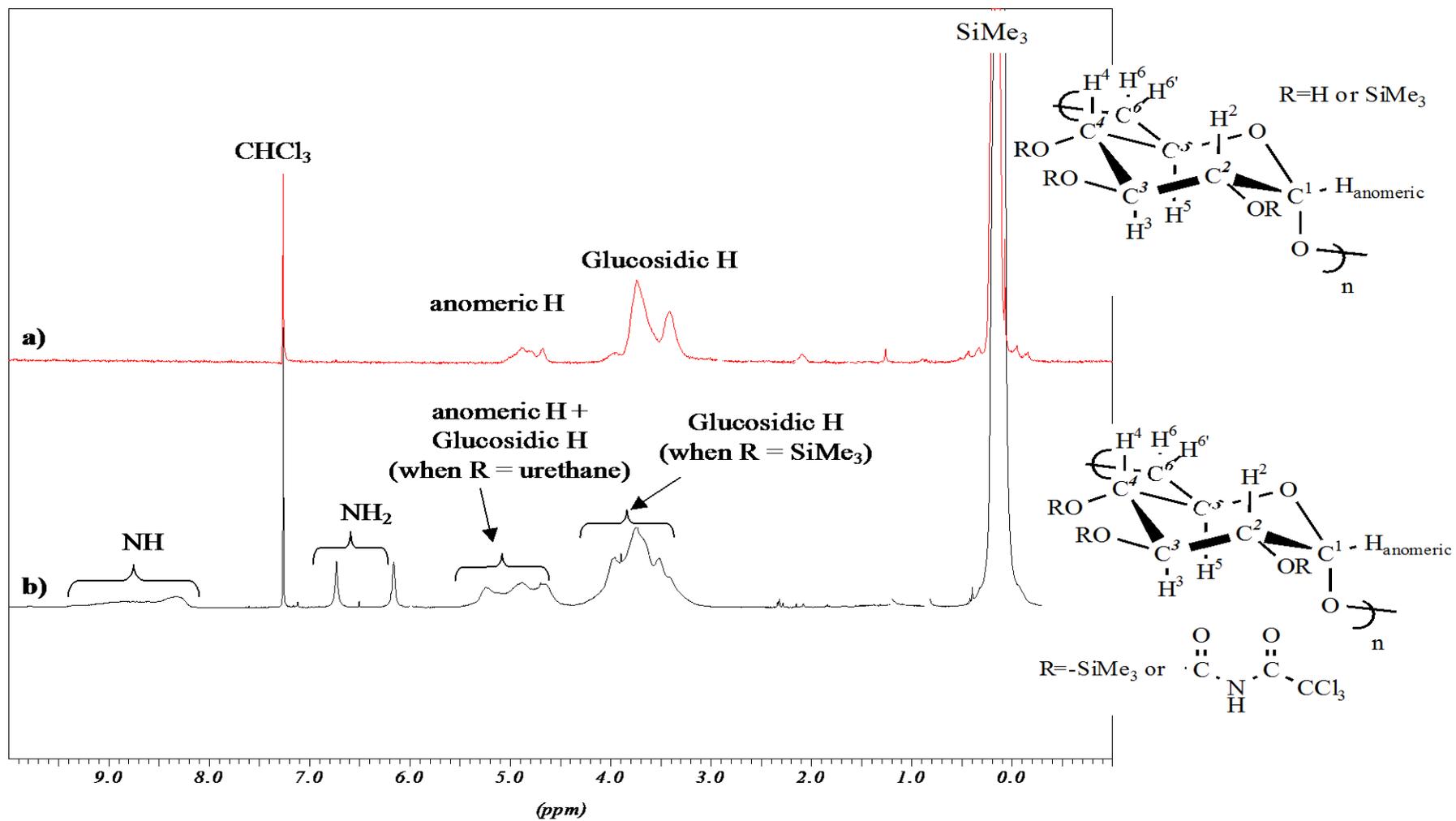
Reactivity of the different dextran alcohol functions towards silylation was studied. As already reported for other reactions, OH<sup>2</sup> is the most reactive function and is the first to get protected. Highly silylated dextran exhibits both complete silylated glucose units and two types of disilylated ones.

### **5) Acknowledgements**

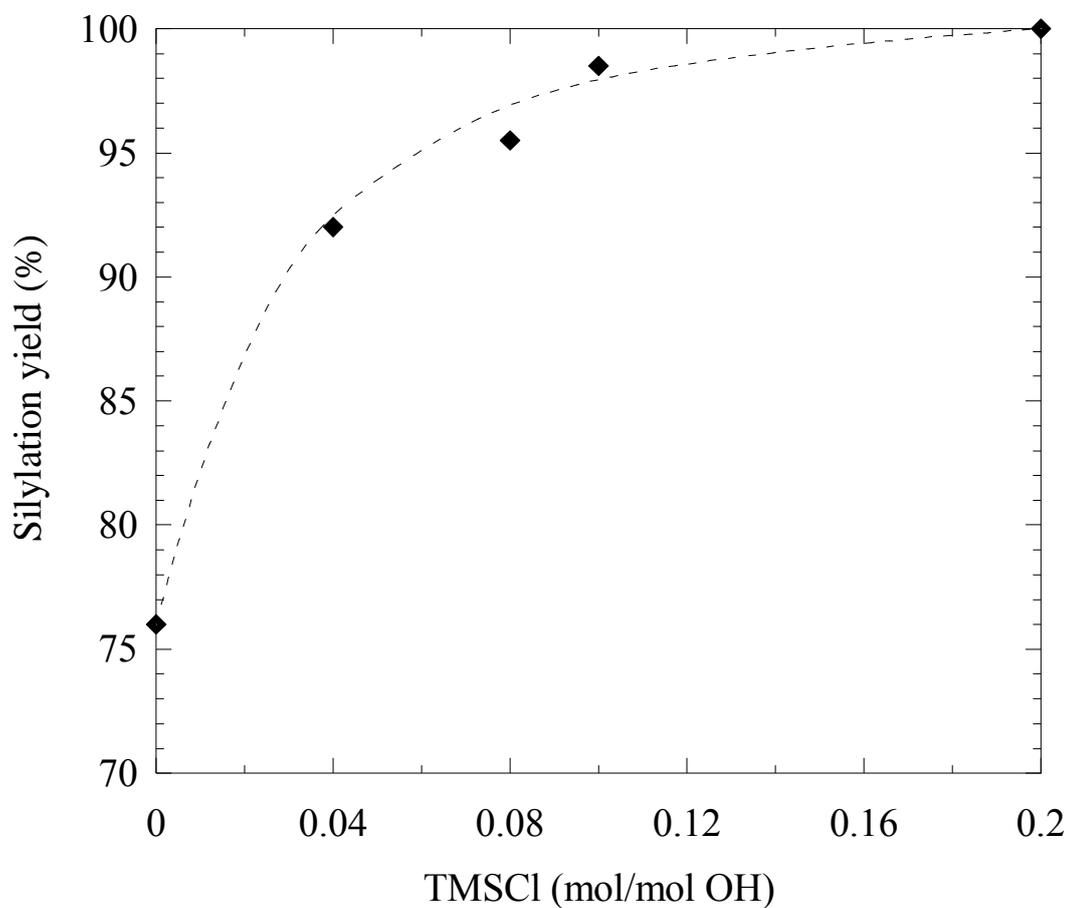
This work was supported by a Tournesol Program for 2000 and 2001 (Tournesol Program N° 00827WH). The authors warmly thank Dr. Marie-Christine Petit and André Vicherat from the same laboratory, for advices in 2D-NMR assignments. LPCM thanks the “Service Fédéraux des Affaires Scientifiques, Techniques et Culturelles” for general support in the frame of the PAI-5/03.



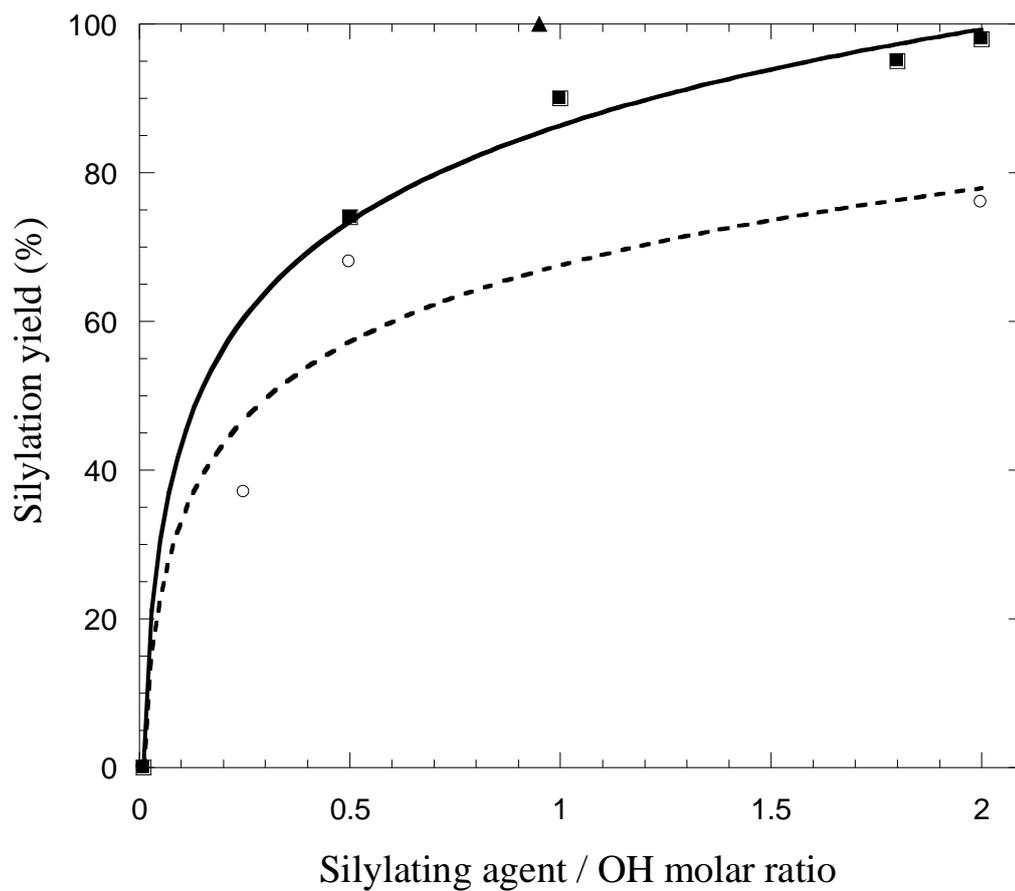
**Figure 1.** Dextran structure



**Figure 2.**  $^1\text{H}$  NMR spectra of partially silylated dextrans ( $\text{CHCl}_3$ ) before (a) and after (b) reaction with trichloroacetylisocyanate.

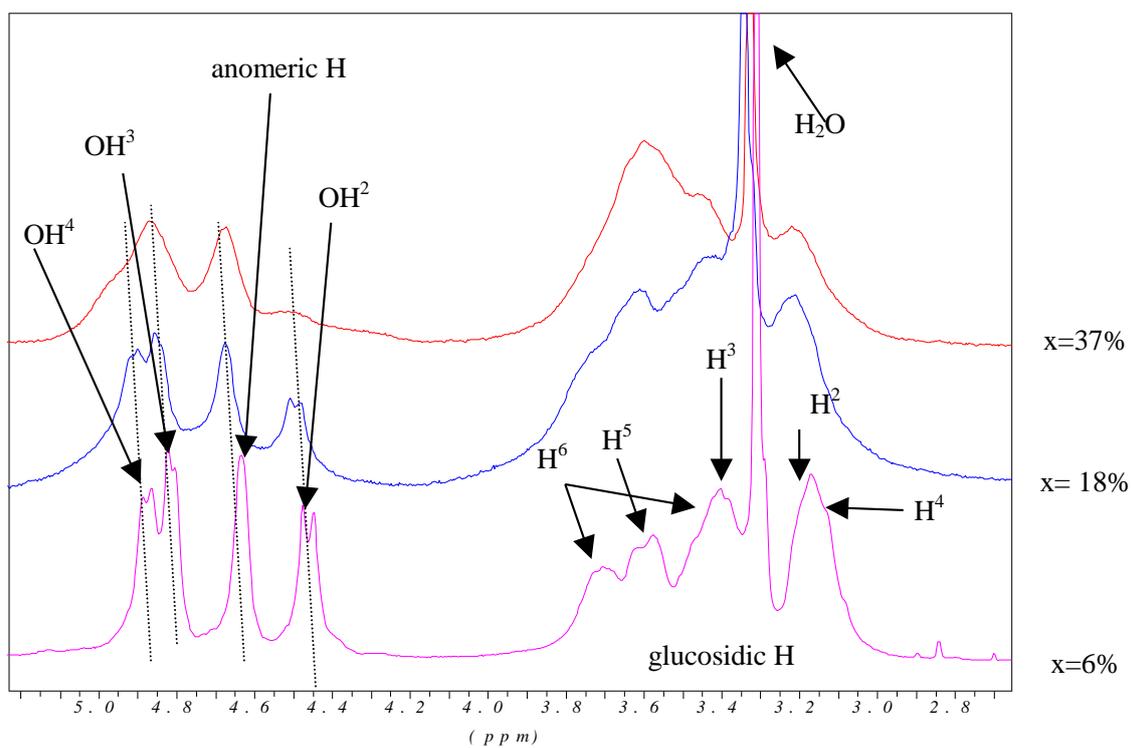


**Figure 3.** Silylation with HMDS + TMSCl : influence of the amount of TMSCl on the silylation yield. Each reaction was carried out in DMSO at 50°C for 20 h using 2 mol total silylating agent per mol OH. Silylation yields were calculated from equation (1).

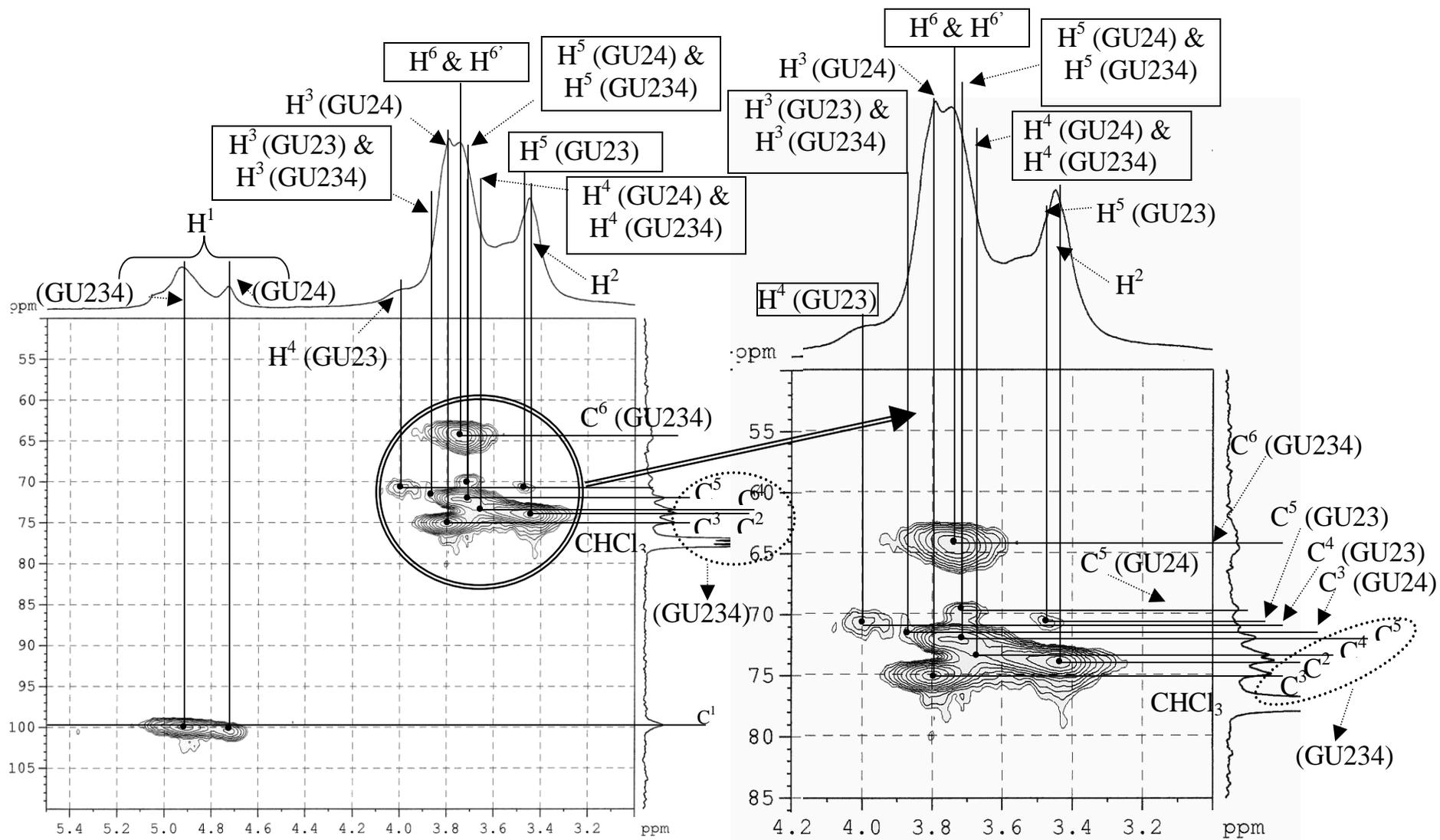


**Figure 4.** Effect of silylating agent/OH molar ratio on silylation yield. Each experiment was carried out in DMSO (except for  $\blacktriangle$ ) at 50°C for 20h.

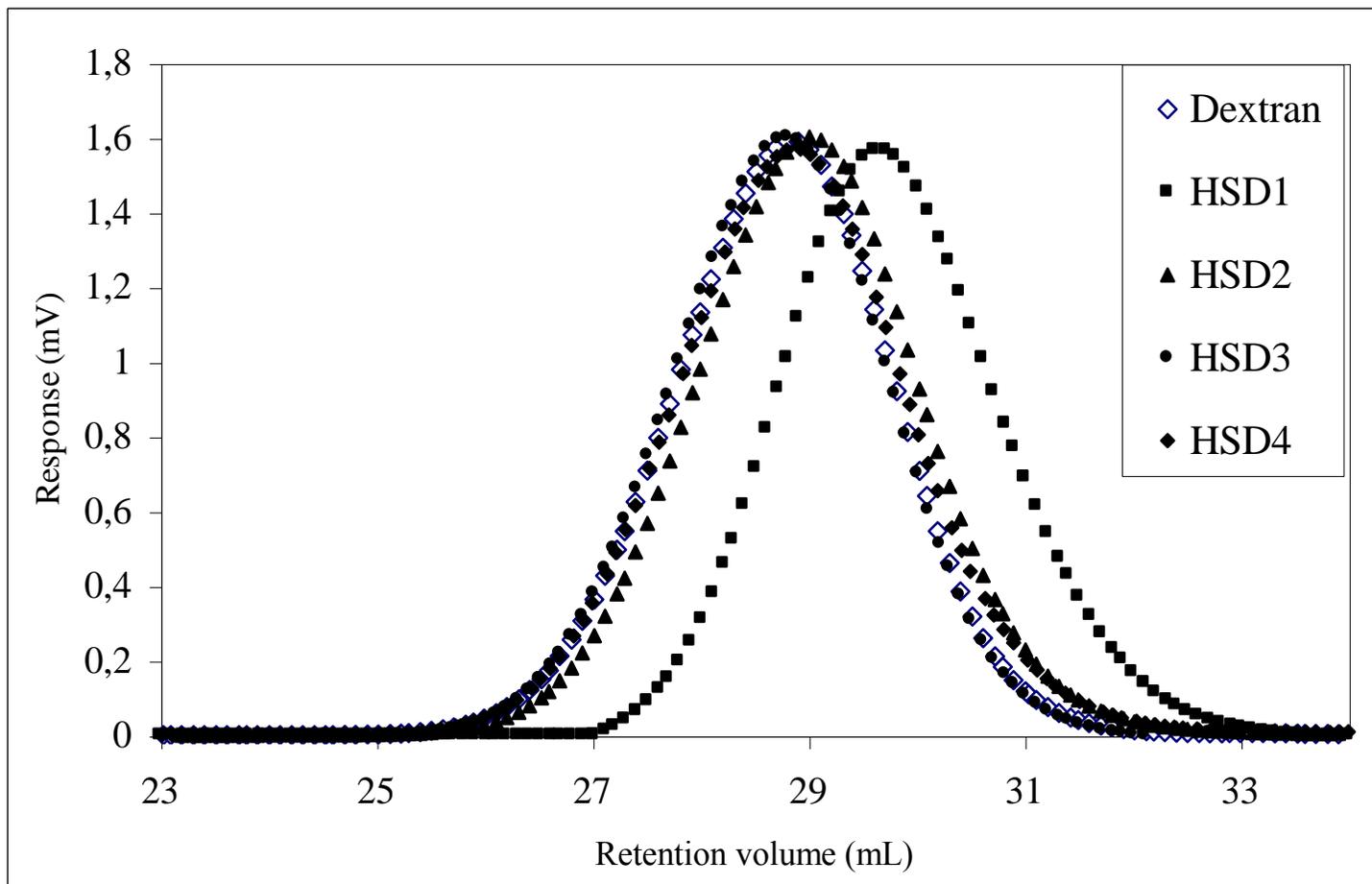
$\blacksquare$  : BSA,  $\circ$  : HMDS,  $\blacktriangle$  : BSA (initial medium = DMSO/toluene (2/1 v/v))



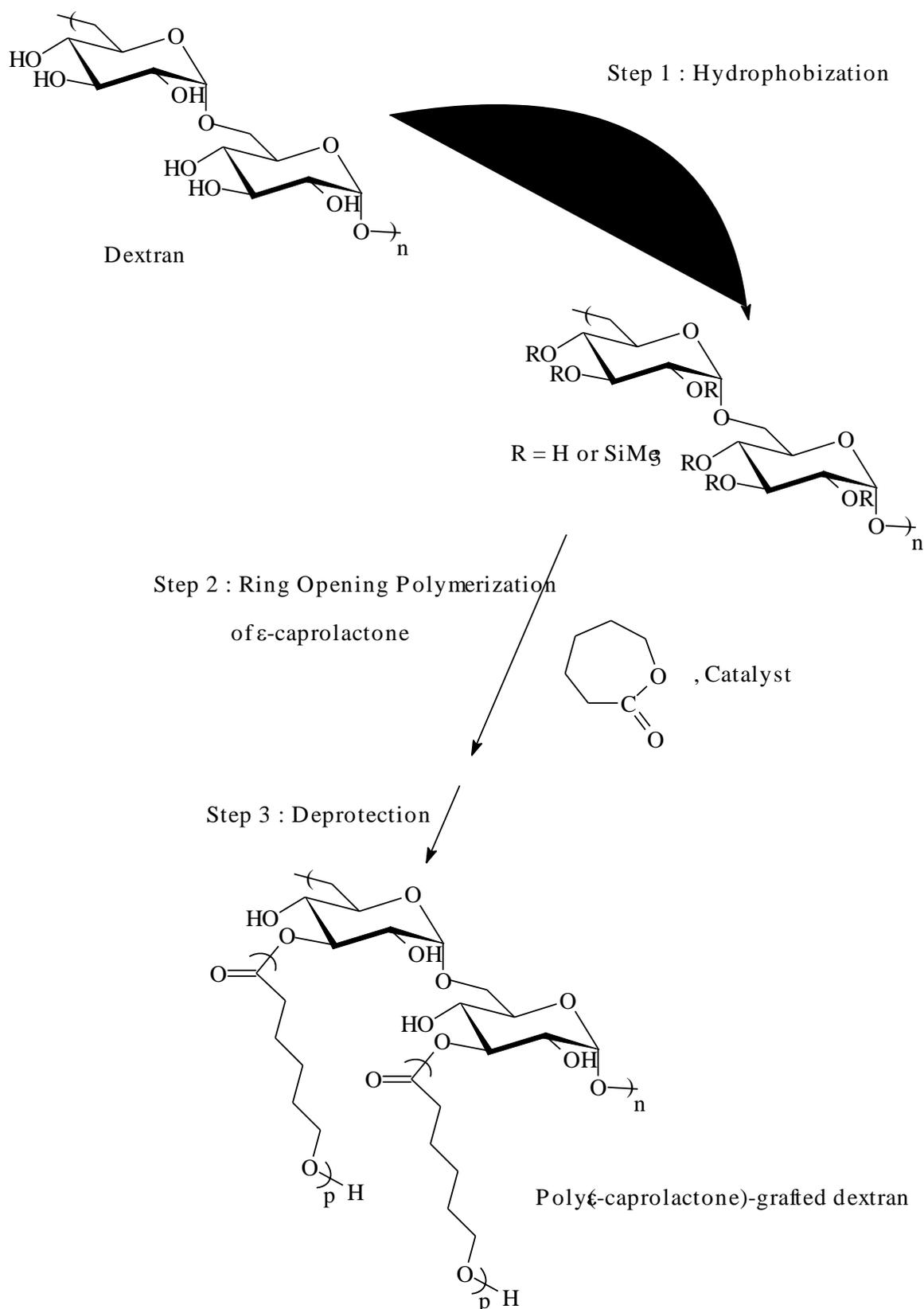
**Figure 5.**  $^1\text{H}$  NMR spectra recorded from 2.6 to 5.2 ppm (in  $\text{DMSO-d}_6$ ) of different silylated dextrans with silylation yield ( $x$ ) varying from 6% to 37%.



**Figure 6.** HMQC spectrum of a 95% silylated dextran ( $\text{CDCl}_3$ ).  $\text{H}^x$  (or  $\text{C}^x$ ) (GUXY(Z)) = proton carried by the carbon  $\text{C}^x$  of a silylated glucose unit on positions X, Y (and Z).

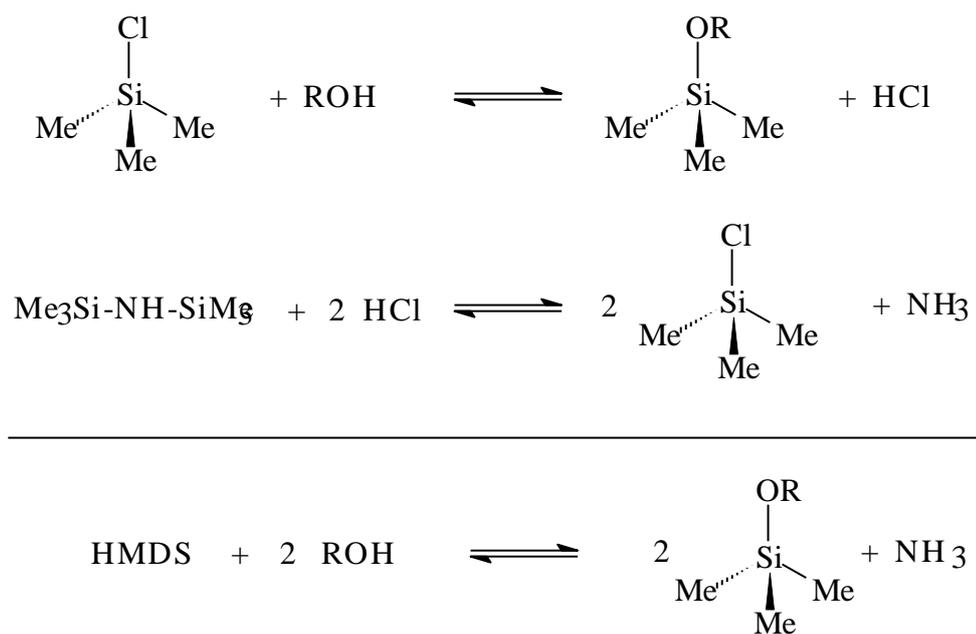


**Figure 7.** Aqueous SEC chromatograms of initial dextran and several silylated dextrans, which have been deprotected (HSD). Silylation reactions [11] were carried out under the following conditions : HSD1 in DMSO with 2 mol HMDS per mol OH at 80°C for 20 h ; HSD2 in DMSO with 2 mol HMDS per mol OH at 50°C for 90 h ; HSD3 in DMSO with (1,8 mol HMDS + 0,2 mol TMSCl) per mol OH at 50°C for 20 h ; HSD4 in a (DMSO/toluene (2/1 v/v)) mixture with 2 mol HMDS per mol OH at 50°C for 20 h.

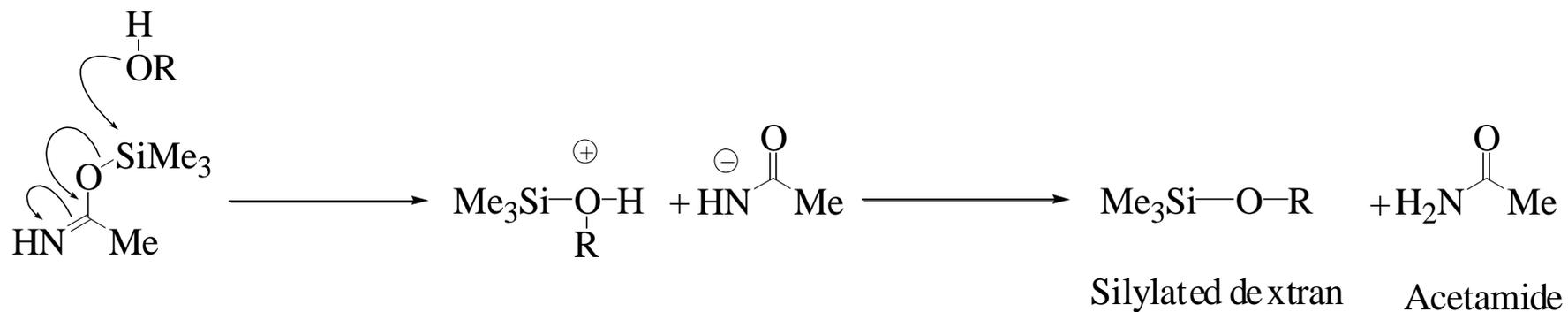
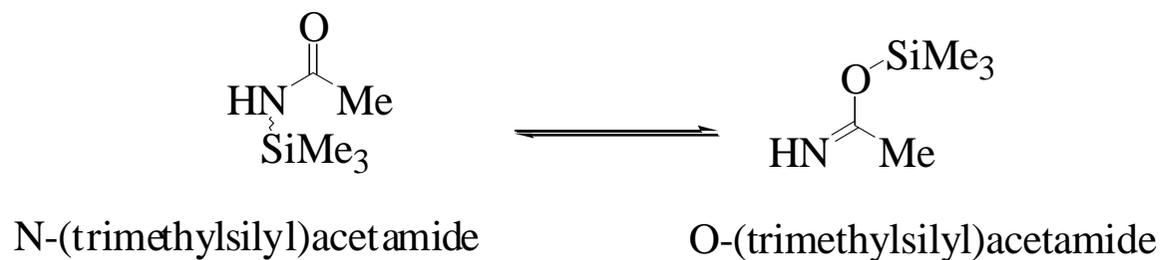
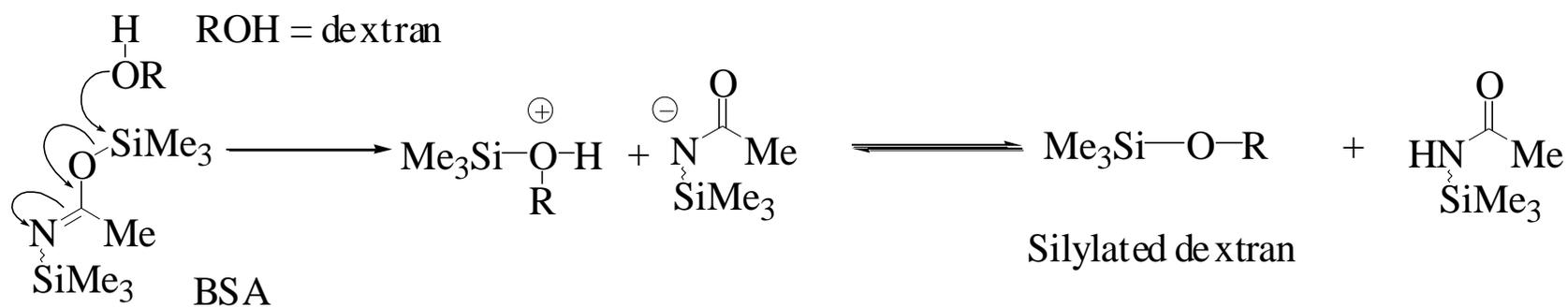


**Scheme 1.** Strategy of poly( $\epsilon$ -caprolactone)-grafted dextran synthesis





**Scheme 3.** Activation of HMDS by TMSCl [14]



**Scheme 4.** Mechanism of the reaction between BSA and dextran

Silylating reagent (mol / mol OH)	Silylation yield (%) <sup>a</sup>
HMDS (2)	76
HMDS (1.8) + TMSCl (0.2)	100
HMDS (2)+ HMPA (0.1)	86
HMDS (2) + NMI (0.1)	77
HMDS (2) + Saccharine (0.1)	90
HMDS (2) + Bu <sub>4</sub> NF (0.1)	88

**Table 1.** Effect of the presence of catalysts on the silylation yield. Each silylation was carried out in DMSO at 50°C for 20 h.

a : calculated from equation (1).

	Silylation solvent	Silylation temperature (°C)	$\overline{M}_n^{\text{d}}$ (g/mol)	I <sup>d</sup>
Dextran			28 900	1.3
HSD5	DMSO <sup>a)</sup>	50	14 800	1.3
HSD6	DMSO <sup>a)</sup>	80	12 600	1.3
HSD7	DMSO/toluene (2/1) <sup>a)</sup>	80	4 900	1.3
HSD8	DMSO <sup>b)</sup>	50	14 200	1.3
HSD9	DMSO <sup>c)</sup>	50	4 100	1.1

**Table 2.** Stability of the dextran chains during the silylation carried out for 20 h using in presence of BSA.

a). 1 mol BSA per mol OH

b). 2 mol BSA per mol OH

c). 3 mol BSA per mol OH

d)  $\overline{M}_n$  = molar mass of silylated dextrans deprotected by HCl/THF as described in the experimental part

## REFERENCES

1. Schuyten, H.A.; Weaver, J.W.; Reid, J.D.; Jurgens, J.F. *J. Am. Chem. Soc.* **1948**, 70, 1919
2. Cooper, G.K.; Sandberg, K.R.; Hinck, J.F. *J. Appl. Polym. Sci.* **1981**, 26, 3827
3. Klebe, J.F.; Finkbeiner, H.L. *J. Polym. Sci., Part A-1* **1969**, 7, 1947
4. Kerr, R.W.; Hobbs, K.C. *Ind. Eng. Chem.* **1953**, 45, 2542
5. Harmon, R.E.; De, K.K.; Gupta, S.K. *Carbohydr. Res.* **1973**, 31, 407
6. Keilich, V.G.; Tihlarik, K.; Husemann, E. *Makromol. Chem.* **1968**, 120, 87
7. Mormann, W.; Demeter, J.; Wagner, T.; *Macromol. Chem. Phys.* **1999**, 200, 693
8. Mormann, W.; Demeter, J. *Macromolecules* **1999**, 32, 1706
9. Mormann, W.; Wagner, T. *Carbohydr. Polym.* **2000**, 43, 257
10. Mormann, W.; Demeter, J. *Macromol. Chem. Phys.* **2000**, 201, 1963
11. Nouvel, C.; Ydens, I.; Degee, Ph.; Dubois, Ph.; Dellacherie, E.; Six, J.-L. *Polymer* **2002**, 43, 1735
12. Ydens, I.; Rutot, D.; Degee, Ph.; Six, J.-L.; Dellacherie, E.; Dubois, Ph. *Macromolecules* **2000**, 33, 6713
13. De Vos, R.; Goethals, E.J. *Polym. Bull.* **1986**, 15, 547
14. Nagy, J.; Borebely-Kuszmán, A.; Becker-Palossy, K.; Zimonyi-Hegedus, E. *Makromol. Chem.* **1973**, 165, 335
15. Corriu, R.J.P.; Dabosi, G.; Martineau, M. *J. Organomet. Chem.* **1978**, 150, 27

16. Little, J.L.; *J. Chromatogr. A.* **1999**, 844, 1
17. El Gihani, M.T.; Heaney, H. *Synthesis* **1998**, 4, 357
18. Tylianakis, M.; Spyros, A.; Dais, P.; Taravel, F.R.; Perico, A. *Carbohydr. Res.* **1999**, 315, 16
19. Haines, A.H. *Adv. Carbohydr. Chem. Biochem.* **1976**, 33, 11
20. Arranz, F.; San Roman, J.; Sanchez-Chaves, M. *Macromolecules* **1987**, 20, 801