Macrocycles. 13.† Stannylenated Glucose Glycosides as Cyclic Initiators of ϵ-Caprolactone and the Synthesis of Biodegradable Networks

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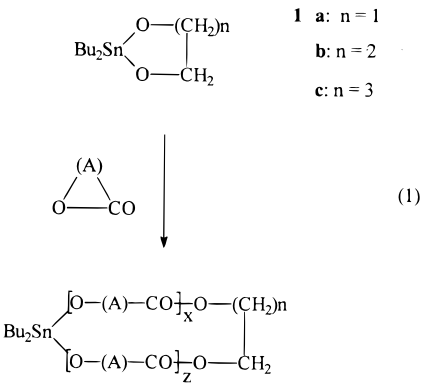
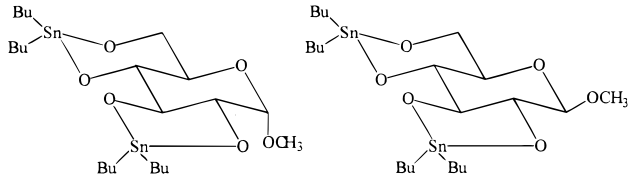
ABSTRACT: The tetraacetates of α- and β-methylglycosides of D-glucose were reacted with dibutyltin dimethoxide in hot toluene with elimination of methyl acetate. The stannylenated glucose derivatives having a five- and six-membered tin-containing ring were isolated in a crystalline form. The soluble α-glycoside was used as cyclic initiator for the polymerization of ϵ-caprolactone at 80 °C. It was found by ^{1}H NMR spectroscopy that the insertion of the lactone exclusively occurs into the six-membered ring at the Sn−O bond of C-6. At prolonged reaction times the stannylenated glucose began to degrade at 80 °C. However, at short reaction times ($t \leq 2$ h) the molecular weight of the macrocyclic polylactone could be controlled by the monomer/initiator ratio (M/I). When sebacoyl chloride was added at the end of the polymerization, all four Sn−O bonds of the active chain end reacted, and swellable, biodegradable networks were obtained. The volume expansion upon swelling depended on the M/I ratio of the ring-opening polymerization and on the solvent.

Introduction

In previous publications[1−5] we have demonstrated that 2-stanna-1,3-dioxacycloalkanes (e.g., **1a**−**c**) and larger Sn−O group containing cycles may serve as initiators for ring-opening polymerizations of lactones. These "macrocyclic polymerizations" yield cyclic oligoesters and polyesters, and no linear species are involved (eq 1). The Sn−O bonds of these tin-containing (super)macrocycles are reactive toward various agents and allow numerous interesting postreactions. For instance, a selective replacement of tin without cleavage of the ring may yield another class of macrocycles.[3] Ring opening with functional acid chlorides or anhydrides yield telechelic oligolactones.[6] Furthermore, the tin-containing (super)macrocycles may serve as bifunctional monomers for ring-opening polycondensations, an approach which may lead to various biodegradable A−B−A−A triblock or multiblock copolymers.[7−9]



The purpose of the present work was twofold. First, a new method allowing for a facile synthesis of the stannylenated D-glucose glycosides **2** and **3** should be elaborated. These glucose derivatives have been mentioned as reactive intermediates in the literature,[10,11] but they have never been isolated. Second, the usefulness of these tricyclic compounds as initiators for polymerizations of lactones should be evaluated. Furthermore, the different reactivities of the Sn−O bonds in the five- and six-membered "tin rings" should be elucidated, and the usefulness of these multifunctional initiators for syntheses of biodegradable networks should be explored.



2 **3**

Experimental Section

Materials. Triethylene glycol, α-D-glucose methylclycoside, β-D-glucose methylglycoside, ϵ-caprolactone, dibutyltin dimethoxide, chloroacetyl chloride, and sebacoyl chloride were all purchased from Aldrich Co. (Milwaukee, WI). The lactone was distilled over freshly powdered calcium hydride in vacuo, and also the acid chloride was distilled before use. The glucose glycosides were acetylated with an excess of acetic anhydride according to ref 12. The tetraacetate of the α-glycoside had a melting point (mp) of 101 °C, and the tetraacetate of the β-glycoside had a mp of 103 °C (mp 102 °C (α) and mp 105 °C (β), respectively, in ref 12).

Stannylenation of Acetylated Triethylene Glycol. Dibutyltin dimethoxide (0.2 mol) and acetylated triethylene glycol (0.2 mol) were mixed together with 20 mL of dry toluene in a round-bottom flask equipped with a condensation bridge. An oil bath temperature of 120 °C was maintained. The liberated methyl acetate was completly removed with the distillation of toluene. Finally, the product was isolated by distillation over a short-path apparatus in a vacuum of 10^{-3} mbar. The properties were identical with those of the previously described product.[5]

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Table 1. ^{1}H NMR Chemical Shifts (in ppm) and Coupling Constants Recorded in $CDCl_3$/TMS

proton position	tetra-*O*-acetyl-α-D-methyl glucopyranoside	bis(2O,-3O-,4O-,6O-dibutyltin) α-D-methyl glucopyranoside	**2** reacted with ϵ-CL (M/I = 20, 80 °C, in $C_2H_2Cl_4$)
$-OCH_3$	3417	3402	3439
	s	s	s
H-1	4960	4787	4793
	d, J = 3.6	d, J = 3.1	d, J = 4.0
H-2	4900	3353	3362
	dd, J = 6.6, 3.6	t, J = 9.7, 8.6	t, J = 9.2, 6.6
H-3	5500	3934	3732
	t, J = 9.9	t, J = 9.7, 10.2	t, J = 9.2
H-4	5070	3578	3532
	t, J = 9.9	t, J = 8.6	enlarged[b]
H-5	3990	3789	3732
	ddd, J = 3.6, 2.5, 2.0	dd, J = 3.6, 6.1	lies under the signal of H-3
H-6	4110	≈3410[a]	4248
	dd, J = 4.6, 2.0	dd, J = 2.3, 3.0	dd, J = 2.0, 10.2
H-6′	4277	3285	4535
	dd, J = 7.6, 4.6	dd, J = 3.1, 6.1	dd, J = 4.1, 8.2

[a] The $-OCH_3$ signal has the same chemical shift. [b] An OH signal has the same chemical shift.

Stannylenation of Tetra-*O*-acetyl-D-methylglucopyranoside (α or *β*). 2,3,4,6-Tetra-*O*-acetyl-D-methylglucopyranoside (0.5 mol) was mixed with 20 mL of dry toluene in a round-bottom flask equipped with a condensation bridge and a dropping funnel. Dibutyltin dimethoxide (0.1 mol) and 15 mL of dry toluene were mixed in the dropping funnel. After the oil bath had reached a temperature of 90 °C the dibutyltin dimethoxide mixture was added slowly to the glycoside while the formed methyl aetate was removed. The product crystallized upon cooling. It was isolated by filtration under inert gas atmosphere and dried at 50 °C in vacuo. Yield (α): 81%; mp: decomposition over 240 °C. Yield (*β*): 58%; mp: decomposition over 240 °C.

^{1}H NMR (α) ($CDCl_3$/TMS): see Table 1.

^{119}Sn NMR (α) ($CDCl_3$/$SnMe_4$): −126.8, −223.7 ppm.

$C_{23}H_{46}O_6Sn_2$ (656.03): Calcd: C, 42.11; H, 7.07. Found (α): C, 42.11; H, 7.14. Found (*β*): C, 42.10; H, 7.15.

Reaction of Bis(2-O, 3-O, 4-O, 6-O-dibutyltin) α-D-Methylglucopyranoside (2) with Dimercaptoethane. Bis-(2-O, 3-O, 4-O, 6-O-dibutyltin) α-D-methylglucopyranoside (0.01 mol) and dry chloroform (30 mL) were heated to 60 °C until the solution was clear. During the dropwise addition of dimercaptoethane (0.022 mol (10% excess)) a white precipitate appeared. The product was isolated by filtration and dried in vacuo. Yield: 98%; mp: 169−170 °C (mp: 169−171 °C, Aldrich).

^{1}H NMR (100 MHz, DMSO-d_6/D_2O): δ = 3.22 ppm (3H, s, $-OCH_3$), δ = 4.50 ppm (1H, d, J = 3.3 Hz, H-1), δ = 3.7−2.9 ppm (6H, m, H-2, H-3, H-4, H-5, H-6).

Specific rotations $[\alpha]^{25}_D$ in deg dm^{-1} g^{-1} cm^3 (H_2O, c = 1 g/dL, l = 1 dm): +157.3 (+157.7, Aldrich).

$C_7H_{14}O_6$ (194.18): Calcd: C, 43.30; H, 7.27. Found: C, 43.18; H, 7.33.

Reaction of Bis(2-O, 3-O, 4-O, 6-O-dibutyltin) α-D-methylglucopyranoside (2) with Chlororacetyl Chloride. Bis(2-O, 3-O, 4-O, 6-O-dibutyltin) α-D-methylglucopyranoside (0.01 mol) and dry chloroform (30 mL) were heated to 60 °C until the solution was clear. A mixture of chloroacetyl chloride (0.044 mol (10% excess)) and dry chloroform (20 mL) was added dropwise, and the solution was refluxed at 70 °C for 2 h. The resulting gray-yellow liquid was stirred at room temperature with the same volume ligroine for 4−5 h. The ligroin phase was decanted and the procedure repeated two times. After removal of the ligroine the resulting white solid was investigated via ^{119}Sn NMR: 128.8 ppm. The chloroform was removed in vacuo, and the resulting gray solid was recrystallized from dry toluene. Yield: 80%; mp: 88−90 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 3.495 ppm (3H, s, $-OCH_3$), δ = 3.92 ppm (1H, dddd, J = 3.0, 2.5, 2.0 Hz, H-5), δ = 3.96−4.18 ppm (8H, m, $-CO-CH_2Cl$), δ = 4.30 ppm (1H, dd, J = 10.2, 2.5 Hz, H-6), δ = 4.372 ppm (1H, dd, J = 8.1, 4.6 Hz, H-6′), δ = 4.90−5.05 ppm (2H, m, H-1, H-2), δ = 5.154 ppm (1H, t, J = 9.7 Hz, H-4), δ = 5.596 ppm (1H, t, J = 9.7 Hz, H-3).

$C_{15}H_{18}Cl_4O_{10}$ (500.11): Calcd: C, 36.02; H, 3.63; Cl, 28.36. Found: C, 36.09; H, 3.74; Cl, 28.10.

Polymerizations of ϵ-Caprolactone with Bis(2-O, 3-O, 4-O, 6-O-dibutyltin) α-D-Methylglucopyranoside. (A) ϵ-Caprolactone (40 mmol) was thermostated to 65 °C in a 50 mL Erlenmeyer flask with silanized glass walls equipped with a reflux condenser. The initiator was dissolved in dry chloroform at the same temperature and added quickly. All polymerizations were performed with the same reaction volume. The resulting polymers were dissolved in CH_2Cl_2, treated with $(SHCH_2)_2$, precipitated from cold diethyl ether, and dried in vacuo at 40 °C.

(B) ϵ-Caprolactone (40 mmol) was thermostated to 80 °C in a 50 mL Erlenmeyer flask with silanized glass walls closed with a glass stopper and steel springs. The initiator was dissolved in dry pyridine at the same temperature and added quickly. The resulting polymer was not worked up.

(C) ϵ-Caprolactone (40 mmol) was thermostated to 80 °C in a 50 mL Erlenmeyer flask with silanized glass walls closed with a glass stopper and steel springs. The initiator was dissolved in dry 1,1,2,2-tetrachloroethane at the same temperature and added quickly. All polymerizations were performed with the same reaction volume. The resulting polymers were dissolved in CH_2Cl_2, precipitated into cold methanol, and dried in vacuo at 40 °C.

Biodegradable Networks. ϵ-Caprolactone (80 mmol) was thermostated to 80 °C in a cylindrical glass reactor (with silanized glass walls) equipped with a mechanical stirrer and gas-inlet and gas-outlet tubes. The initiator **2** was dissolved in 8 mL of 1,1,2,2-tetrachloroethane and added quickly. After a poylmerization time of 2 h the sebacoyl chloride was added and stirred for another hour at 80 °C. After cooling to room temperature the resulting gel was washed four times with dry CH_2Cl_2 and dried for 3 days in vacuo at 40 °C.

To determine the swelling factors, the dry gels were weighed (0.1 g) into graduated glass tubes and covered with the corresponding solvent. After 24 h the remaining solvent was decanted, and the volume of the swelled gels was measured by adding 5 mL of dry diethyl ether.

Measurements. The inherent viscosities were measured with an automated Ubbelohde viscometer thermostated at 25 °C. The 400 MHz ^{1}H NMR spectra were recorded on a Bruker AM-400 FT NMR spectrometer in 5 mm o.d. sample tubes using $CDCl_3$/TMS as solvent and shift reference. The 134.3 MHz ^{119}Sn NMR spectra were recorded with a Bruker AM-360 FT NMR spectrometer in 10 mm o.d. sample tubes in $CDCl_3$ using $SnMe_4$ as internal shift reference.

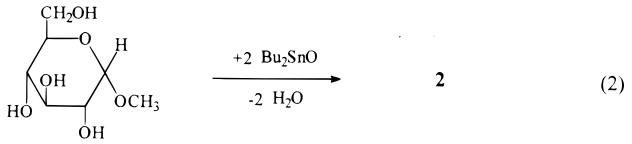
The DSC measurements were obtained on a Perkin-Elmer DSC-7 apparatus in aluminum pans under nitrogen at a heating rate of 20 °C/min.

The GPC measurements were conducted at 30 °C with a Kontron HPLC/GPC apparatus equipped with a Waters differential diffractometer Md 410. Four Ultrastyragel columns with pore sizes of 10^2, 10^3, 10^4, and 10^5 Å were used, and tetrahydrofuran served as eluent.

The optical rotaions were determined with a Perkin-Elmer polarimeter Md 421 in a cuvette of 10 cm length.

Results and Discussion

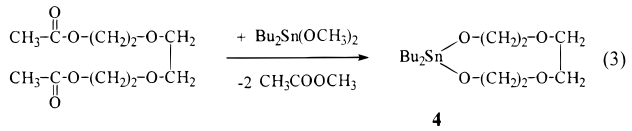
Syntheses. The synthesis of the bis-stannylenated α-glycoside (bis(2-O, 3-O, 4-O, 6-O-dibutyltin) α-D-methylglucopyranoside) **2** was performed in the literature[10] by the reaction of α-D-glucose methylglycoside with dibutyltin oxide in refluxing toluene (eq 2). This procedure is simple, but it has the following disadvantages. First, it is the reaction between two solid materials. Second, when we synthezised the 2-stanna-1,3-dioxepane **1c** analogously from dibutyltin oxide and 1,4-butanediol, we found that the distilled product contains



(2)

several percent of free CH_2OH groups, even when a slight excess of Bu_2SnO was used. With dibutyltin dimethoxide as reaction partner of 1,4-butanediol this contamination was not observed.

The new synthetic method described in this work had the purpose to avoid any free OH groups and to use soluble and meltable reaction partners. Taking into account that tin alkoxides react easily with sterically nonhindered ester groups by transesterification,[13] a model reaction between dibutyltin dimethoxide and acetylated triethylene glycol was studied (eq 3). Triethylene glycol as reaction partner had the advantage that a stable monomeric product was formed which was known from a former study.[9] Furthermore, the singlet signals of both acetate and methoxide groups were clearly observed in the ^1H NMR spectra and allowed an easy monitoring of the conversion.



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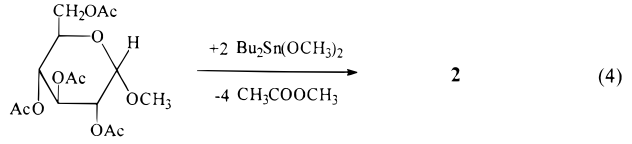
The complete conversion according to eq 3 suggested that this approach might be useful to prepare the stannylenated glucose glycosides **2** and **3** in a pure form from their well-known tetraacetates according to eq 4.



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The syntheses of **2** and **3** were conducted in concentrated toluene solutions, and the liberated methyl acetate was completly removed with the distilling reaction medium. The stannylenated α-glycoside **2** precipitated from the reaction mixture upon cooling in the form of a white crystalline powder, whereas **3** began to precipitate during the condensation. The lower solubility of **3** in all inert solvents was confirmed by separate studies with the isolated compound. A low solubility was only found in hot (>100 °C) tetrachloroethane. But under these conditions **3** began to decompose so that no satisfactory NMR spectra were obtained. This low solubility of **3** prevented any further characterization in solution and studies of chemical reactions.

The α-glycoside derivative **2** showed a moderate solubility in warm chlorobenzene and a better solubility in warm chloroform, 1,2-dichloroethane, and 1,1,2,2-tetrachloroethane (>50 °C). The good solubility in chloroform allowed ^1H and ^{119}Sn NMR measurements and allowed us to perform chemical reactions. The ^{119}Sn NMR spectrum exhibited to sharp signals at −126.8 and −223.7 ppm (relative to internal $SnMe_4$), indicating the existence of donor−acceptor interactions between O and Sn atoms. From literature data[14] it is known that a chemical shift of −126 ppm is characteristic for a pentacoordinated Bu_2Sn group, whereas a signal above −220 ppm is typical for a hexacoordinated one. Furthermore, it is well-known from **1a** and **1b** and several dibutyltin derivatives of saccharides[10,15−18] that five- and six-membered 2-stanna-1,3-dioxa alkanes form fairly stable dimers via intermolecular association. Therefore, it is obvious that **2** and **3** form at least dimers such as **5**. The different solubilities of **2** and **3** can be explained by the assumption that in the case of **3** also the six-membered ring is engaged in a fairly stable intermolecular association so that a polymeric associate is formed in the solid state. In the case of **2** this intermolecular association may be weaker due to an intramolecular interaction involving the α-glycoside oxygen and the Sn of the six-membered ring. The ^1H NMR spectrum of **2** (Figure 1B) displayed the expected upfield shift (0.6−0.9 ppm) of all protons neighboring the Sn−O groups relative to those of the tetraacetate (Figure 1A).

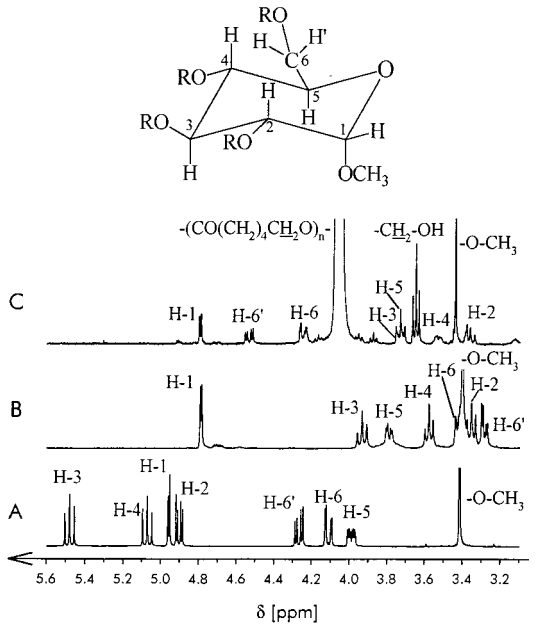
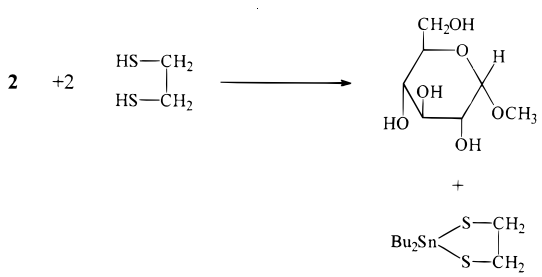


Figure 1. The 400 MHz ^1H NMR spectra of (A) 2,3,4,6-tetra-*O*-acetyl-α-D-methylglucopyranoside, (B) bis(2-O, 3-O, 4-O, 6-O-dibutyltin) α-D-methyl-glucopyranoside **2**, and (C) **2** after the reaction with ϵ-CL (M/I = 20, 80 °C in 1,1,2,2-tetrachloroethane).

In the framework of this study two reactions of **2**, namely with 1,2-dimercaptoethane and with acid chlorides, were of interest. When a solution of **2** in warm chlorobenzene or chloroform was treated with an equimolar amount of dimercaptoethane, the α-D-glycoside was liberated in a yield of 98 ± 1% (eq 5). The optical rotaion of the reaction product was identical with that of the starting material. This result means that a quantitative removal of the dibutyltin group is feasible without affection of the glycoside structure, and it means that the combination of stannylation and mercaptolysis can be used as a nonaqueous saponification of saccharide acetates.



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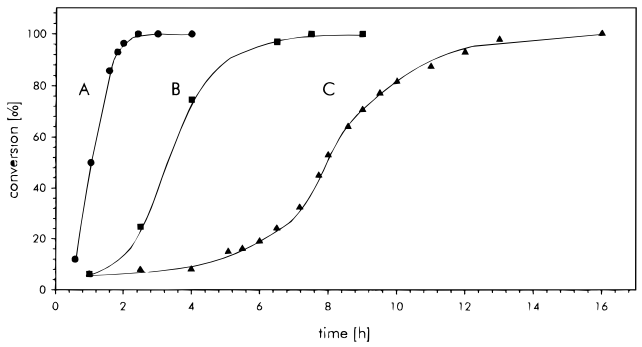

Figure 2. Time−conversion curves for **2**-initiated polymerizations of ϵ-CL (M/I = 40) in concentrated solutions: (A) in 1,1,2,2-tetrachloroethane at 80 °C, (B) in pyridine at 80 °C, and (C) in chloroform at 65 °C.

The second reaction consisted in the treatment of **2** with chloroacetyl chloride to find out whether all four Sn−O bonds can be acetylated. A solid product giving satisfactory elemental analyses was obtained, and the ^{1}H NMR spectrum confirmed the 4-fold acetylation. However, the ^{1}H NMR spectrum also suggested a partial anomerization. This result was not unexpected since anomerization is known to be catalyzed by nonaqueous protic acids and Lewis acids.

Polymerizations. Preliminary experiments (not described here in detail) proved that **2** can in principle be used as an initiator for polymerizations of ϵ-caprolactone (ϵ-CL) in bulk at temperatures ≥60 °C. However, the poor solubility of **2** in ϵ-CL prevented any control of the molecular weight via the M/I ratio. Therefore, all further polymerizations were conducted in solution. A first series of measurements were conducted in refluxing chloroform (65 °C). The time−conversion curve (C, in Figure 2) recorded for a M/I ration of 40 revealed that despite this high initiator concentration a time of 15 h is required for an almost complete conversion. Therefore, much longer reaction times were expected for higher M/I ratios, and thus, all further polymerizations were performed at a higher temperature (i.e., 80 °C). Because of a moderate (but sufficient) solubility of **2** in 1,1,2,2-tetrachloroethane and pyridine (in contrast to other inert solvents), theses solvents were preferentially used, and it was hoped that pyridine will break up the association formulated in formula **5**, thereby accelerating the polymerization of ϵ-CL. However, the time−conversion curves illustrated in Figure 2A,B demonstrate that the polymerization in pyridine was considerable slower. Therefore, all preparative polymerizations of ϵ-CL were finally performed in 1,1,2,2-tetrachloroethane at 80 °C (Tables 2 and 3). The time−conversion curves of Figure 3 illustrate that the overall reaction rates depend as expected on the M/I ratio, or in other words, they depend on the concentration of the initiator. Even in the least favorable case (i.e., M/I = 150) a complete conversion was observed after 2.25 h.

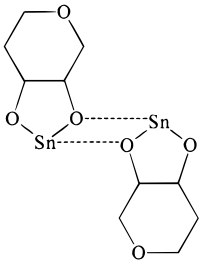

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Table 2. 2-Initiated Polymerizations of ϵ-Caprolactone at 80 °C in 1,1,2,2-Tetrachloroethane (Precipitated into Cold Methanol)

no.	M/I	t (h)	yield (%)	η_{inh} (dL/g)[a]	$M_{n,theor}$[b]	M_n (GPC)[c]	M_n (GPC)[d]
1	20	3	85	0.16	2300		
2	40	3.5	90	0.23	4600		
3	60	3.5	94	0.26	6900	6500	10000
4	100	5	94	0.31	11400	9000	12500
5	150	6	96	0.36	17000	11500	16500

[a] Measured at 25 °C with c = 2 g/L in CH_2Cl_2. [b] Calculated from the M/I ratio and 100% conversion. [c] GPC measurements in THF at 30 °C calibrated with the M.-H. equation (7). [d] GPC measurements in THF at 30 °C calibrated with the M.-H. equation (8).

Table 3. 2-Initiated Polymerizations of ϵ-Caprolactone at 80 °C in 1,1,2,2-Tetrachloroethane (Precipitated into Cold Methanol)

no.	M/I	t (h)	yield (%)	η_{inh} (dL/g)[a]	$M_{n,theor}$[b]	M_n (GPC)[c]	M_n (GPC)[d]
1	20	1	88	0.15	2300		
2	40	1	60	0.18	4600		
3	60	1.5	85	0.26	6900	6500	9600
4	100	2	89	0.32	11400	13000	20700
5	150	2	88	0.42	17000	16600	25600

[a] Measured at 25 °C with c = 2 g/L in CH_2Cl_2. [b] Calculated from the M/I ratio and 100% conversion. [c] GPC measurements in THF at 30 °C calibrated with the M.-H. equation (7). [d] GPC measurements in THF at 30 °C calibrated with the M.-H. equation (8).

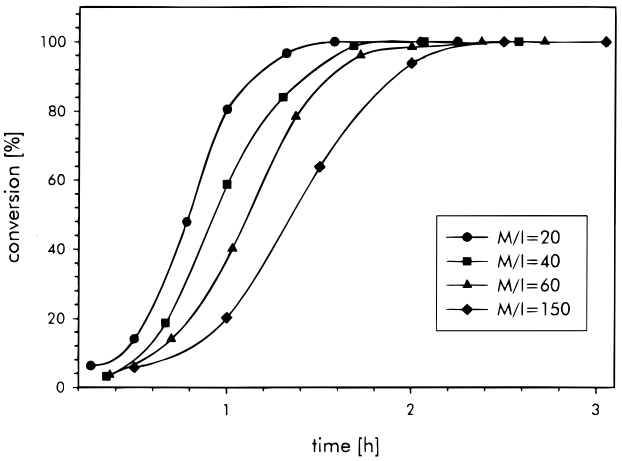
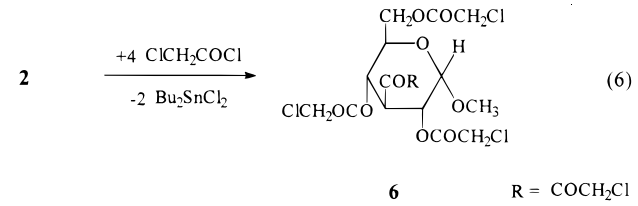


Figure 3. Time−conversion curves for **2**-initiated polymerizations of ϵ-CL in 1,1,2,2-tetrachloroethane at 80 °C with variation of M/I ratio.



2 +4 $ClCH_2COCl$, -2 Bu_2SnCl_2 → **6**, R = $COCH_2Cl$ (6)

A series of preparative polymerizations were again conducted with variation of the M/I ratio, and the polylactones were isolated by precipitation into cold methanol. The saccharide end groups of the isolated polylactones were characterized by ^{1}H NMR spectroscopy. As illustrated in Figure 1C, only the protons of C-6 displayed the downfield shift expected for an acylation of the neighboring oxygen by ϵ-CL. This observation was made for the polymers of both series, and the signal pattern did not not change with the M/I ratio. Therefore, it may safely be concluded that the insertion

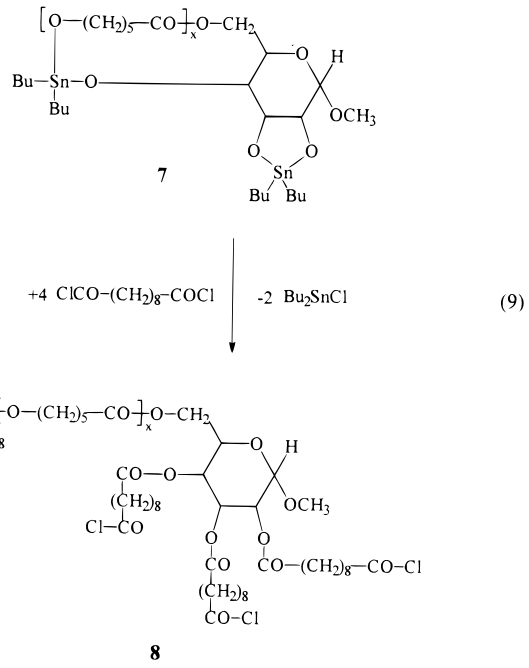
of ϵ-CL exclusively occurs into the six-membered ring at the Sn−O bond of C-6. In other words, the virgin reaction products have all the structure **7**. This result is reasonable because reactions at the six-membered Sn ring is sterically less hindered, and a higher nucleophilicity of the oxygen at C-6 is well documented for numerous reactions in the glucose chemistry.

When the inherent viscosities and the molecular weights obtained by GPC measurements were analyzed, the following results were found. The viscosities and molecular weights increased with higher M/I ratios, in agreement with a living polymerization according to structure **7**. However, a comparison of the inherent viscosities with those of an **1c**-initiated polymerization (published previously[4]) suggested that the molecular weights obtained with M/I 100 or 150 were too low for a clean polymerization process. The number-average molecular weights (M_ns) derived from GPC measurements evaluated with the "*K*" and "*a*" values of the Mark−Houwink equation (7)[19] confirmed this conclusion. In this connection it should be mentioned that the evaluation of GPC measurements by means of polystyrene standards or by the "*K*" and "*a*" values of eq 8 (determined for polystyrene in THF at 30 °C)[20] is the international standard. However, we have previously demonstrated[4] that the calibration with the polystyrene values of eq 8 overestimates the molecular weights of poly(ϵ-CL) by 40−100% (depending on the M_n). In contrast, the calibration with eq 7 determined by Schindler et al.[19] for poly(ϵ-CL) in THF gave reasonable results.

$$[\eta] = 1.395 \times 10^{-4} M^{0.786} \quad (7)$$

$$[\eta] = 1.25 \times 10^{-4} M^{0.717} \quad (8)$$

Originally, it was suspected that the lower than expected molecular weights might result from a partial hydrolysis and methanolysis during the workup procedure. Therefore, all polymerizations were repeated, and the workup procedure was changed. 1,2-Dimercaptoethane was added to the CH_2Cl_2 solutions of the polylactones for a complexation of the tin, and the polylactones were precipitated into dry diethyl ether. The yields and viscosities obtained in this way were almost identical with those listed in Table 2, confirming the lower than expected molecular weights. Furthermore, a slow increase of the number of CH_2−O−Sn (or CH_2−OH after precipitation into methanol) end groups was observed with longer reaction times. This observation cannot be explained by backbiting degradation. As a consequence of these results, the stability of the initiator **2** was checked in 1,1,2,2-tetrachloroethane at 80 °C, and a slow degradation was observed. Therefore, another series of polymerizations were performed with shortest possible reaction times allowing for a nearly complete conversion. These reaction times, 1 h for the lowest M/I ratio and 2 h for the highest, were derived from the time−conversion curves of Figure 3. With these shorter times satisfactory results were obtained as indicated by the viscosities and M_n values summarized in Table 3. In other words, when stannylenated glucose **2** is used as initiator, the reaction time is crucial for the success of the polymerizations in contrast to the use of **1c** or similar thermostable initiators. In summary, the **2**-initiated polymerizations allow a satisfactory control of the molecular weights via the M/I ratios under carefully optimized reaction conditions.



7

8

Networks

The results described above indicated that the poly(ϵ-CL) chains formed at relatively low M/Is ($\leq$150), and short reaction times (t $\leq$ 2 h) have the tricyclic structure **7**. As demonstrated by the model reaction of **2** with chloroacetyl chloride all four Sn−O bonds of the glucose derivative should react with acid chlorides, although only C-6 is reactive enough toward ϵ-CL. This structure offers the chance for an "in situ" synthesis of biodegradable networks by addition of a dicarboxylic acid chloride to the reaction mixture of the polylactones. (Equation 8 represents a first stage of this process.) This means that the *r*ing-*op*ening *p*olymerization of ϵ-CL is directly combined with an in situ *poly*condensation, a synthetic approach we have previously "nicknamed" the ROPPOC method (or strategy).[9] ROPPOC syntheses were designed previously to yield soluble multiblock copolymers; the syntheses conducted in the present study had the purpose to yield insoluble networks with a systematic variation of the segment lengths and, thus, of the pore sizes.

All cross-linking experiments were conducted at 80 °C by addition of sebacoyl chloride, and a rapid increase of the viscosity followed by gelation was observable after complete addition of the acid chloride. The resulting gels were intensively extracted with dichloromethane to remove all the liberated dibutyltin dichloride and possibly unreacted ϵ-CL. After drying and weighing, the DSC measurements of all gels were conducted. As illustrated by the DSC traces of Figure 4 and by the DSC data listed in Table 4, the linear chain segments were indeed able to crystallize, and both the melting temperature (T_m) and the crystallinity decreased with lower M/I ratios or, in other words, with a higher density of cross-links. Finally the solid gels were exposed to different solvents to study the swelling effect. The data listed in Table 5 show that the volume expansion indeed increases with the M/I ratio used for the polymerization of ϵ-CL; they also prove that the quality of the solvation plays a role with CH_2Cl_2 being the best solvent. Hence, the properties of these gels confirm that the **2**-initiated

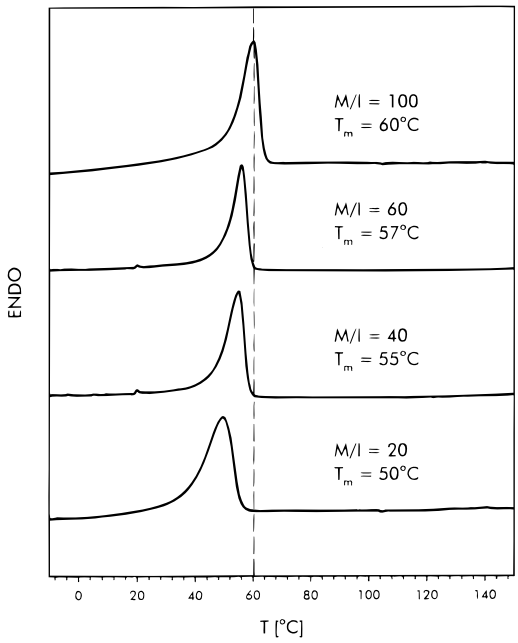


Figure 4. DSC measurements (second heat) of the biodegradable networks.

Table 4. DSC Measurements of the Biodegradable Networks

no.	M/I	T_m (°C)	ΔH (J/g)
1	20	50	43
2	40	55	46
3	60	57	48
4	100	60	49

Table 5. Results from the Swelling Experiments of the Biodegradable Networks

no.	M/I	solvent	SF[a]	no.	M/I	solvent	SF[a]
1	20	toluene	6	9	20	THF	10
2	40	toluene	9	10	40	THF	10
3	60	toluene	11	11	60	THF	13
4	100	toluene	15	12	100	THF	14
5	20	CH_2Cl_2	9	13	20	DMF	9
6	40	CH_2Cl_2	12	14	40	DMF	<3
7	60	CH_2Cl_2	15	15	60	DMF	<3
8	100	CH_2Cl_2	19	16	100	DMF	<2

[a] SF = swelling factor.

polymerization allowed a proper control of the average molecular weights of the chain segments.

Conclusion

The experiments of the present work indicate that the transesterification of acetylated glucose glycoside with dibutyltin dimethoxide is a quantitative reaction that allows the synthesis of tricyclic dibutyltin derivatives of glucose in high yields. Strong donor−acceptor interactions between Sn−O groups strongly reduce the solubility of these dibutyltin derivatives (**2** and **3**) and hinders a broader preparative use of the β-glycoside (**3**). The more soluble α-glycoside (**2**) proved to be useful as initiator for ϵ-CL, and at short reaction times the molecular weight of the resulting poly(ϵ-CL) can be controlled by the M/I ratio. Only one of the four Sn−O bonds, namely the most reactive one at C-6, proved to be involved in the polymerization process. The in situ combination of the ring-opening polymerization with a polycondensation based on dicarboxylic acid chlorides offers an easy access to biodegradable gels which might be useful for controlled drug release.

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