Macromolecular Engineering of Polylactones and Polylactides. 23. Synthesis and Characterization of Biodegradable and Biocompatible Homopolymers and Block Copolymers Based on 1,4,8-Trioxa[4.6]spiro-9-undecanone

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ABSTRACT: Homopolymers of 1,4,8-trioxa[4.6]spiro-9-undecanone (TOSUO) and block copolymers of TOSUO and ϵ-caprolactone (ϵ-CL) have been synthesized with aluminum isopropoxide as an initiator in toluene at 25 °C. The homopolymerization is first order with respect to both monomer and initiator, and the end-group analysis agrees with a coordination−insertion mechanism based on the acyl-oxygen cleavage of the TOSUO ring. Living poly(ϵ-caprolactone) (PCL) and poly(1,4,8-trioxa[4.6]spiro-9-undecanone) (PTOSUO) chains are very efficient macroinitiators for the polymerization of TOSUO and ϵ-CL, respectively, with formation of block copolymers of a narrow molecular weight distribution. Size-exclusion chromatography (SEC) and ^{13}C-NMR confirm the blocky structure of the copolymers, in agreement with DSC, which shows two glass transitions characteristic of the amorphous phase of PCL and PTOSUO, respectively. The ethylene ketal pendent groups of the PTOSUO block have been successfully converted to ketones and hydroxyl pendent groups without scission of the polyester backbone. These new materials have potential for applications in medicine, surgery, and tissue engineering.

Introduction

Aliphatic polyesters, such as polylactones, polylactides, and polyglycolide, have received steadily increasing attention for applications in medicine and surgery over the past 20 years. This interest is due to a valuable set of properties, e.g. resorption after an appropriate period of implantation time, nontoxicity for living organisms and good ultimate mechanical properties.[1] These aliphatic polyesters are well-known for their *in vitro* as well as *in vivo* hydrolytic degradation with release of nontoxic byproducts.[2] They display a large range of biodegradability: their half-life time can vary from several days to several years, and the copolymerization of the parent monomers is an easy way to adjust more precisely the rate of biodegradation.[1]

Several years ago, some of us reported that the living polymerization of ϵ-CL could be promoted by aluminum alkoxides, such as bimetallic (Zn,Al) μ-oxo alkoxides[3,4] and trialkoxyaluminum.[5] The living polymerization of ϵ-CL has also been reported by Inoue[6] and Penczek[7] using ($\alpha,\beta,\gamma,\delta$-tetraphenylporphinato)aluminum ([TPP]-AlX) derivatives and diethlyaluminum methoxide, respectively, as initiators. Furthermore, Hamitou et al. took advantage of the bimetallic μ-oxo alkoxides in order to synthesize block copolymers of ϵ-CL and β-propiolactone (β-PL).[8] It is worth noting that substitution of the alkoxide functions by a hydroxylated prepolymer, such as ω-hydroxylpolystyrene (PS) or -polybutadiene (PBD), provides a direct access to the related PS (or PBD)−PCL diblock copolymers.[9] More recently, our laboratory has launched a research program dealing with the macromolecular engineering of polylactones and polylactides. Aluminum alkoxides, such as $Al(O^iPr)_3$ and $Et_{3-p}Al(O(CH_2)_2X)_p$ with $3 \geq p \geq 1$, have proved to be very effective initiators for the polymerization of lactones, lactides, glycolide, and cyclic anhydrides. Polymerization is typically "living" and allows block copolyesters with perfectly controlled molecular weight and composition to be prepared. Aluminum alkoxides carrying functional alkoxy groups (X = Br, CH_2NEt_2, $CH_2CH{=}CH_2$, $OC(O)C(Me){=}CH_2$, etc.) are at the origin of asymmetric telechelic polyesters including polyester macromonomers (end groups being X and OH, respectively).[24] Coupling the asymmetric telechelic chains via the hydroxyl end group or better its Al alkoxide precursor is a straightforward way to symmetric telechelic polyester and star-branched polyester bearing the X functional end group.[25,26]

Nowadays, attention is paid to synthetic aliphatic polyesters bearing functional pendent groups with the idea of attaching drugs, regulating cell activity, improving surface hydrophilicity, etc. The typical pathway to functional polyester is based on functional monomers, which are prone to polymerization or copolymerization with lactones or lactides. The functional groups must be selected or previously protected in such a way that they do not interfere with the polymerization mechanism. Synthesis of some polyesters bearing functional pendent groups has been reported.[10−23] However, the functional monomer is usually prepared according to a rather complex and time-consuming recipe, resulting in poor yields. In almost all the cases, polymerization of the functional monomers is out of control (not "living").

This paper deals with the polymerization of 1,4,8-trioxa[4.6]spiro-9-undecanone (or 5-ethylene ketal ϵ-caprolactone) (TOSUO) initiated by aluminum isopropoxide and the synthesis and characterization of block copolymers of TOSUO and ϵ-CL, in which ketone pendent groups can be released by the complete deacetalization of the PTOSUO block and also completely reduced to hydroxyl pendent groups without scission of the polyester backbone. The very straightforward and high-yield synthesis of TOSUO must be emphasized and makes the parent polymer a very attractive precursor of hydroxyl-containing polyester.

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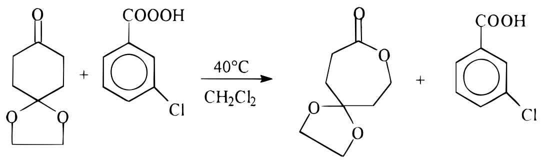
Experimental Section

Materials. The synthesis of 1,4,8-trioxa[4.6]spiro-9-undecanone (TOSUO) was described elsewhere.[27] Equation 1 shows the synthesis pathway. TOSUO was dried by repeated (three times) azeotropic distillation of toluene just before polymerization. Triphenylcarbenium tetrafluoroborate (ACROS), sodium borohydride (Janssen), and ethanol (Riedel-de Haën) were used as received. ϵ-Caprolactone (ϵ-CL) (Janssen) was dried over calcium hydride for 48 h at room temperature and distilled under reduced pressure just before use. Toluene (ACROS) was dried by refluxing over calcium hydride and distilled under a nitrogen atmosphere. Dichloromethane (ACROS) was dried over molecular sieves (Aldrich) and distilled just before use. Aluminum isopropoxide [$Al(O^iPr)_3$] (Aldrich) was twice sublimated and then dissolved in toluene under nitrogen.



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Polymerization Techniques. Block copolymerization was carried out as follows. Polymerization of ϵ-caprolactone (or TOSUO) was initiated with $Al(O^iPr)_3$ in toluene at 25 °C. An aliquot of the "living" poly(ϵ-caprolactone) (or PTOSUO) solution was picked out, deactivated, and precipitated in cold heptane for analysis by size-exclusion chromatography (SEC) and ^{1}H-NMR. A known amount of the solution of TOSUO (or ϵ-CL) in toluene was transferred to the "living" polymer solution. The final copolymer was deactivated by an excess of 1 N HCl solution and precipitated in cold heptane.

Deacetalization of Block Copolymers. ϵ-CL/TOSUO block copolymer (2.4 mmol of TOSUO) and triphenylcarbenium tetrafluoroborate (2.5 mmol) were dissolved under stirring for 30 min in 100 mL of dichloromethane (3 wt % copolymer). Then copolyester A was recovered by precipitation in cold methanol.

Reduction of Ketone Pendent Groups into Hydroxyl Groups. Copolyester A (1.2 mmol of ketone) and sodium borohydride (1.45 mmol) were dissolved under stirring in a CH_2Cl_2/EtOH (5/2 v/v) mixture (ca. 1.0 wt % copolymer) for 30 min. Then copolyester B was recovered by precipitation in cold methanol.

Characterization. ^{1}H-NMR spectra of polyesters were recorded in $CDCl_3$ at 400 MHz in the FT mode with a Bruker AN400 superconducting magnet system. IR spectra were recorded with a Perkin-Elmer 106 FTIR. Size-exclusion chromatography (SEC) was performed in THF by using a Hewlett-Packard 1090 liquid chromatography equipped with a Hewlett-Packard 1037 A refractometer index detector and a set of four columns (pore size: 10^5, 10^3, 500, and 100 Å). Molecular weight and molecular weight distribution were calculated by reference to a universal calibration curve set up with polystyrene (PS) standards and the PS and PCL viscosimetric relationships.[9] Molecular weights were also calculated by ^{1}H-NMR from the relative intensity of the signals of the isopropyl ester end group (δ = 5.01 ppm) and the methylene groups in the chain (δ = 4.16 or 1.98 ppm). ϵ-CL/TOSUO block copolymers were characterized by SEC and their compositions determined by ^{1}H-NMR from the signal intensities of the poly(ϵ-caprolactone) methylene groups (δ = 4.06 or 1.65 ppm) and the polyTOSUO methylene groups (δ = 4.16 or 1.96 ppm), respectively. From the overall composition and M_n of the first polymerized block (SEC and/or ^{1}H-NMR), the molecular weight of the second block was calculated. Differential scanning calorimetry (DSC) was carried out with a DuPont 910 DSC thermal analyzer calibrated with indium. The melting temperature (T_m) and melting enthalpy (ΔH_m) were measured after cooling the sample to −120 °C and heating it up to 100 °C (at a 20 °C/min rate). The glass transition temperature (T_g) was measured for samples premelted at 100 °C for 1 min, quenched to −120 °C, and then heated at a 20 °C/min rate. Thermogravimetric analysis was carried out with a TA 51 thermogravimetric analyzer over the 25−600 °C temperature range at a 10 °C/min scan rate under nitrogen.

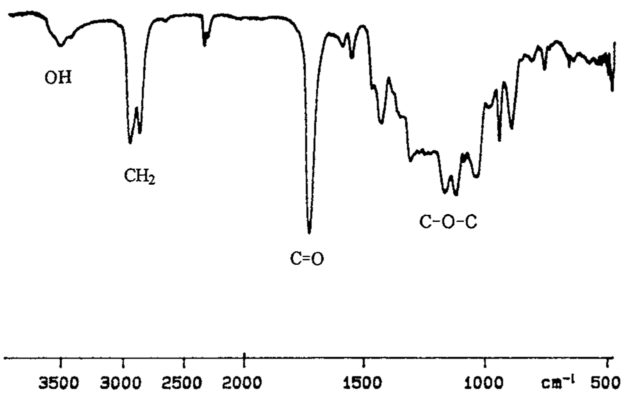


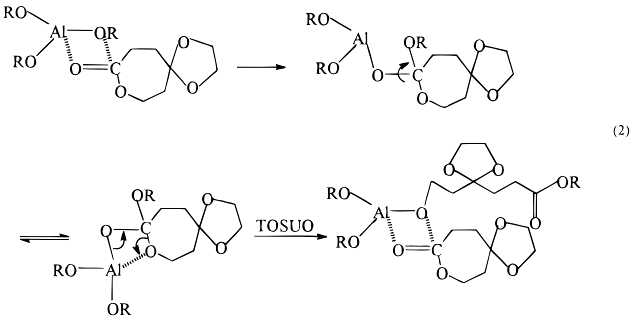
Figure 1. IR spectrum of poly(TOSUO).

Results and Discussion

Homopolymerization of TOSUO Initiated by Aluminum Isopropoxide. It was previously shown that aluminum isopropoxide was very efficient in promoting the living polymerization of ϵ-caprolactone in toluene at 0 °C and (D,L and L,L) lactides (LA) in toluene at 70 °C.[5,28] The polymerization mechanism clearly proceeds through the coordinative insertion of the monomer into an aluminum alkoxide bond of the initiator. This insertion involves the selective cleavage of the acyl-oxygen bond of the monomer and it accordingly controls the nature of the polyester end groups, i.e., an ester and a hydroxyl group, respectively.

Structural similarities between TOSUO and ϵ-CL might suggest that the two monomers are polymerized according to the same mechanism. In order to confirm this hypothesis, known amounts of $Al(O^iPr)_3$ and TOSUO were reacted in toluene at 25 °C. After hydrolysis, the final products were quantitatively recovered by precipitation in heptane, purified, and analyzed by IR and ^{1}H-NMR spectroscopies. The IR spectrum (Figure 1) shows a broad absorption in the region of 3500 cm^{-1}, which is characteristic of the hydroxyl functions. Furthermore, the absorption at 914 cm^{-1} typical of the TOSUO monomer has completely disappeared. The ^{1}H-NMR spectrum (Figure 2) shows that the reaction product contains as many hydroxyl groups (δ = 3.75 ppm; H_f) as isopropyl ester groups (δ = 5.01 ppm; H_b). No carboxylic acid proton can be observed.

On the basis of these observations and by analogy with the mechanism accepted for ϵ-CL and LA polymerization initiated by aluminum alkoxides, eq 2 schematizes the TOSUO ring-opening polymerization. Indeed coordination of $Al(O^iPr)_3$ to the exocyclic carbonyl oxygen of TOSUO, followed by the acyl-oxygen cleavage



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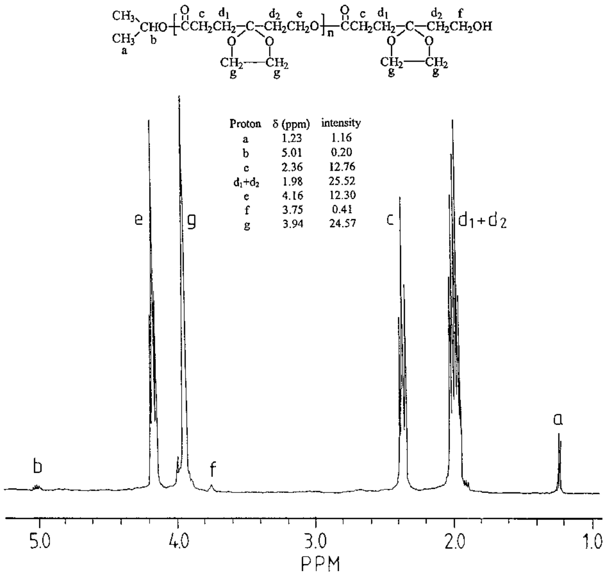


Proton	δ (ppm)	intensity
a	1.23	1.16
b	5.01	0.20
c	2.36	12.76
d_1+d_2	1.98	25.52
e	4.16	12.30
f	3.75	0.41
g	3.94	24.57

Figure 2. ^{1}H-NMR spectrum of poly(TOSUO) in $CDCl_3$.

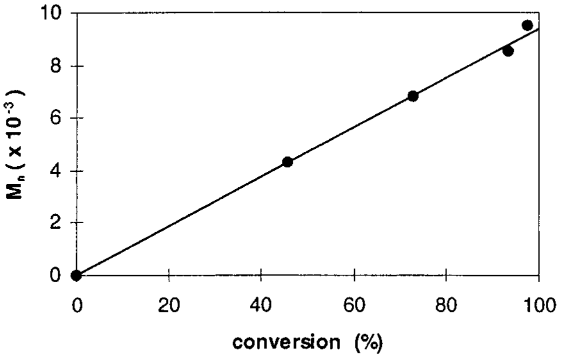


Figure 3. Relationship between M_n and monomer conversion for the TOSUO polymerization initiated by $Al(O^iPr)_3$ (A3) in toluene at 25 °C.

of the monomer accounts for an isopropyl ester end group, (multiplet at 5.01 ppm (H_b) and a doublet at 1.24 ppm (H_a) in a 1:6 ratio, Figure 2). Deactivation of the living polyester chains with dilute HCl converts the propagating aluminum alkoxide group into a hydroxyl group. The methylene protons (H_f) of this CH_2OH end group are clearly observed as a triplet at 3.75 ppm.

Living Polymerization of TOSUO. The TOSUO polymerization is perfectly "living" when initiated by $Al(O^iPr)_3$ in toluene at 25 °C. Figure 3 shows indeed that the molecular weight of PTOSUO linearly increases with the monomer conversion. Furthermore, there is a close agreement between the mean degree of polymerization (DP) at total conversion (^{1}H-NMR and/or SEC) and the monomer/initiator molar ratio (Figure 4). Finally, the molecular weight distribution of PTOSUO is rather narrow (M_w/M_n = 1.15−1.25), in agreement with a fast initiation compared to propagation and a fast propagation compared to transfer or termination reaction if any.

Average Number of Active Sites. In toluene, $Al(O^iPr)_3$ forms tetrameric (A4) and/or trimeric (A3) aggregates, which are dissociated upon the addition of the cyclic monomer.[29−31] Actually, LA is responsible for the complete deaggregation of both A_3 and A_4 into single species (A_1) trisolvated by the monomer (Al coordination number CN = 6).[31] In contrast, A_3 is preferentially deaggregated by ε-CL, as supported by kinetic analysis, which has concluded that the initiation rate constant with A3 is 10^3 times larger than with A4.[30] This behavior accounts for an apparent average number of active sites of 1.0 in the case of ε-CL. Whatever the monomer, three chains are thus initiated by the active A_1 species.[31] In this study, the A3 content of the initiator solution was measured by NMR,[30,31] and Figure 4 shows that the dependence of DP versus the initial [monomer]/(3[A_3]) molar ratio is linear (slope = 1/3). Therefore, three PTOSUO chains are initiated per $Al(O^iPr)_3$ molecule involved in the trimeric aggregates, so that the molecular weight (M_n) can be predicted by eq 3, where M_T is the molecular mass of TOSUO (172 g/mol), α is the monomer conversion, and [A3] is the initial concentration of $Al(O^iPr)_3$ trimers.

$$M_n(\text{theor}) = ([\text{TOSUO}] \times M_T \times \alpha)/(9[\text{A3}]) \quad (3)$$

Similarly to ε-CL, TOSUO thus dissociates preferentially the A3 aggregates of $Al(O^iPr)_3$ in toluene.

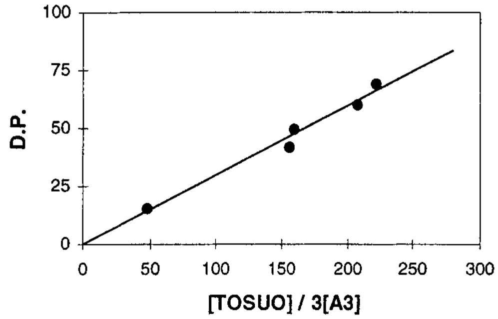


Figure 4. Dependence of the average degree of polymerization (DP) on the initial monomer/initiator molar ratio for the TOSUO polymerization initiated by $Al(O^iPr)_3$ (A3) in toluene at 25 °C.

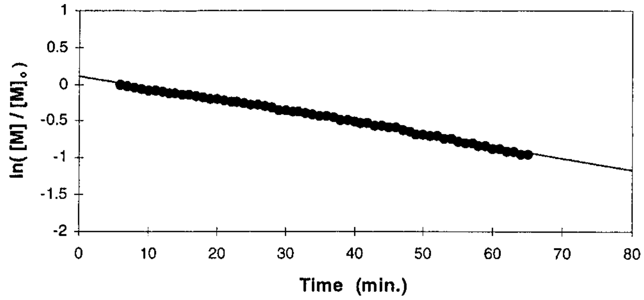


Figure 5. Linear dependence of the monomer consumption on the polymerization time. $[M]_0$ = initial monomer concentration and [M] = monomer concentration at time *t*.

Polymerization Kinetics. The kinetics of the TOSUO polymerization was studied by dilatometry in toluene at 25 °C. Figure 5 shows a linear time dependence of the monomer consumption, which is in agreement with a living polymerization of a first order in monomer. The same kinetic feature has previously been reported for the ε-CL and LA polymerization initiated by $Al(O^iPr)_3$.[5,28] An induction period of ca. 3−6 min is observed when monomer and initiator are mixed together, so that the straight line does not go through the origin of the $\ln([M]/[M]_0)$ versus time plot. This induction period actually corresponds to the time required for the dissociation of the $Al(O^iPr)_3$ aggregates.[31]

A linear relationship is also observed when the apparent rate constant ($k_{app} = \ln([M]/[M]_0)/t$) is plotted as a function of the initiator concentration $[Al(O^iPr)_3]$ (Figure 6). Thus, the TOSUO polymerization is also first order in initiator.

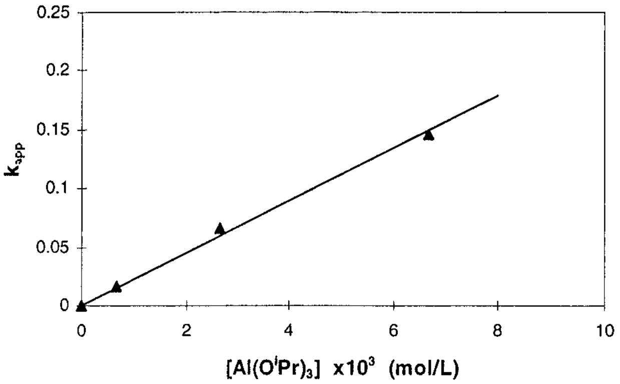


Figure 6. Linear dependence of the apparent rate constant (k_{app}) on the initiator concentration [Al(O^{i}Pr)$_3$].

In conclusion, except for the induction period, the ring-opening polymerization fits the following overall kinetic law:

$$-\mathrm{d[TOSUO]}/\mathrm{d}t = k\mathrm{[TOSUO][Al(O^iPr)_3]} \qquad (4)$$

where the kinetic constant k = 21 L·mol^{-1}·min^{-1} (obtained from the slope of Figure 6). This equation is exactly the same as for polymerization of ε-CL and LA in toluene at 0 and 70 °C, respectively. k values are then 36.6 L·mol^{-1}·min^{-1} for ε-CL[5] and 0.6 L·mol^{-1}·min^{-1} for LA.[28] Compared with ε-CL (0 °C), the TOSUO polymerization (25 °C) is thus slower, although the difference is not dramatic.

Block Copolymerization of TOSUO and ε-CL. In contrast to random copolymers, block and graft multicomponent systems are most often multiphase materials, which accounts for the additivity of the constitutive phase properties. Furthermore, di- or triblock copolymers are potential interfacial agents in immiscible polymer blends. This emulsification strategy is useful to improve the phase morphology, the interfacial adhesion, and, accordingly, the ultimate mechanical properties of multiphase blends. When two or more monomers can be polymerized in a living manner according to the same mechanism, their sequential polymerization is a unique way to prepare block copolymers. As shown in the previous section, TOSUO comply to the same "coordination−insertion" polymerization as ε-CL, which is the prerequisite for the straightforward synthesis of diblock and even triblock copolymers of TOSUO and ε-CL.

Diblock copolymers have been prepared with either living PCL or living PTOSUO chains as macroinitiators. Synthesis of triblock copolymers of ε-CL and TOSUO has also been successfully achieved. The typical SEC chromatograms for block copolymers are shown in Figure 7. The molecular weight distribution for the first block is narrow and does not change significantly upon the second and the third block formation, whereas no homopolymer formation can be detected by SEC. As expected, the molecular weight of the macroinitiator is systematically shifted toward higher values, in agreement with the theoretical values. Results and conditions for the block copolymerization are reported in Table 1. It must be noted that the initial monomer concentration (whatever it is) is 1.0 mol·L^{-1} in all the experiments. When the TOSUO polymerization is initiated by living PCL chains of M_n = 10000 (expected M_n(PTOSUO) = 8200), the monomer conversion at 25 °C is only 32% after 16 h. In contrast, the ε-CL conversion (expected M_n(PCL) = 13500) at 25 °C is complete for the same period of time (17 h) when initiated by living PTOSUO chains of M_n = 12700. This difference is consistent with the polymerization rate constants for TOSUO (21 L·mol^{-1}·min^{-1}) at 25 °C and for ε-CL (36.6 L·mol^{-1}·min^{-1}) at 0 °C. Indeed, the k value for the ε-CL polymerization in toluene at 22 °C is as high as 165 L·mol^{-1}·min^{-1} when calculated from the polymerization activation energy,[33] i.e. at least 8 times larger than k for TOSUO at the same temperature in the same solvent.

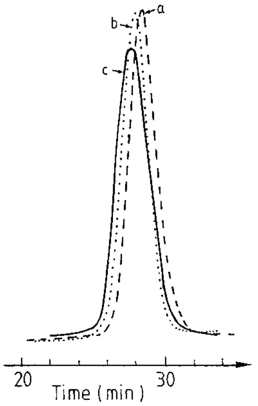


Figure 7. SEC chromatograms of block copolymers: (a) the first block, PCL, M_n = 2800; (b) poly(ε-CL-*b*-TOSUO), M_n = 2800/2000; (c) poly(ε-CL-*b*-TOSUO-*b*-ε-CL), M_n = 2800/2000/1000.

Figures 8 and 9a show the IR and ^{1}H-NMR spectra for a typical poly(ε-CL-*b*-TOSUO). In order to assess that the copolymerization product is a pure diblock, i.e., that no transesterification has occurred between the PCL and PTOSUO blocks, a ^{13}C-NMR spectrum was recorded. ^{13}C-NMR spectroscopy is a method very sensitive to the chemical environment of the studied nucleus and it is accordingly a powerful tool to analyze

Table 1. Block Copolymerization of ε-CL and TOSUO Initiated by Al(O^{i}Pr)$_3$ in Toluene at 25 °C

block copolyester	$M_n{}^a$ (theor)	polym time (h)	conv (%)	M_n (exp)	$M_n{}^b$(SEC)	M_w/M_n (SEC)
PCL block	10.0K	0.33	100	9.2K	9.2K	1.20
PCL/PTOSUO	10.0K/7.5K	0.33/2.2	11	9.2K/0.75K	8.5K	1.25
PCL block	10.0K	0.25	100	8.8K	8.8K	1.20
PCL/PTOSUO	10.0K/8.2K	0.25/16	32	8.8K/2.5K	6.9K	1.35
PTOSUO block	12.7K	7.25	100	12.4K	5.6K	1.25
PTOSUO/PCL	12.7K/13.5K	7.25/17	100	12.4K/14.8K	11.3K	1.35
PCL block	2.8K	0.22	100	2.9K	2.9K	1.20
PCL/PTOSUO	2.8K/2.1K	0.22/0.55	100	2.9K/2.0K	3.7K	1.20
PCL/PTOSUO/PCL	2.8K/2.1K/1.2K	0.22/0.55/0.67	100	2.9K/2.0K/1.0K	3.8K	1.25
PCL block	8.1K	0.25	100	8.4K	8.4K	1.10
PCL/PTOSUO	8.1K/6.0K	0.25/24	100	8.4K/5.6K	10.2K	1.20
PCL/PTOSUO/PCL	8.1K/6.0K/6.5K	0.25/24/4.3	100	8.4K/5.6K/6.9K	15.9K	1.20

[a] Theoretical molecular weight calculated with eq 3; K stands for thousand. [b] M_n(SEC) based on polystyrene standards with the universal calibration for PCL.[9]

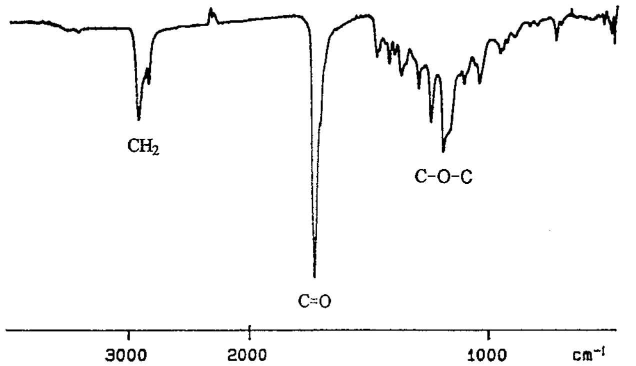


Figure 8. IR spectrum of poly(ϵ-CL-*b*-TOSUO) copolymer (M_n = 2800/2000).

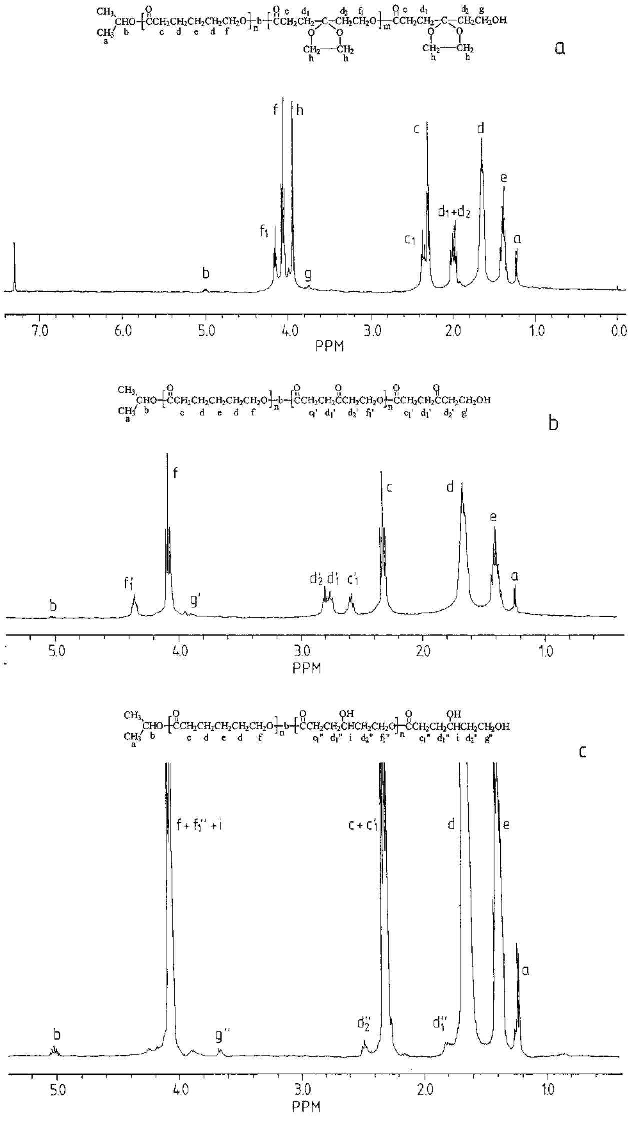


Figure 9. ¹H-NMR spectrum of poly(ϵ-CL-*b*-TOSUO) copolymer (M_n = 2800/2000): (a) before deacetalization; (b) after deacetalization; (c) after reduction.

the actual average length of each type of monomer sequence in copolymers. We have shown elsewhere that ^{13}C-NMR of poly(ϵ-CL-*co*-TOSUO) random copolymers based on the carbonyl signals is a very suitable analytical method.[32] For the ϵ-CL/TOSUO block copolymers, transesterification reactions must result in mixed sequences, easily detected by an additional resonance in between the homodiad peaks in the carbonyl region. Figure 10 confirms the absence of any additional intermediate peak in this region. Only the two homodiad peaks (Figure10b) are observed at the chemical shifts characteristic of each homopolymer (Figure 10a,c).

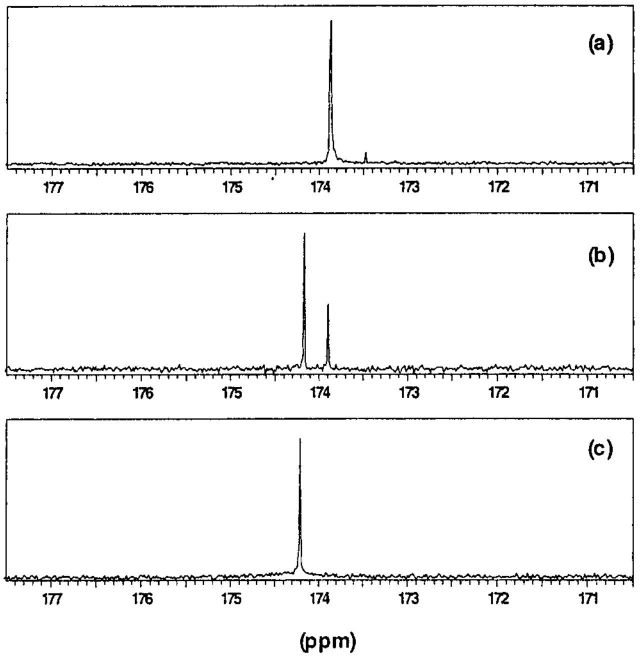
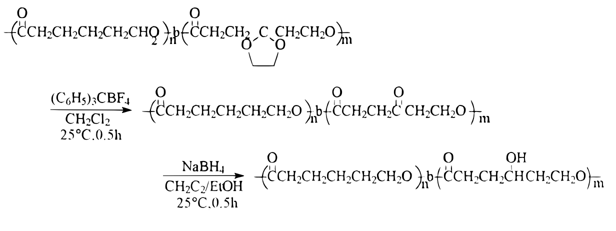


Figure 10. Expanded ^{13}C-NMR spectra (carbonyl region) of (a) PTOSUO, (b) poly(ϵ-CL-*b*-TOSUO), and (c) PCL.

Deacetalization of Poly(TOSUO) and Reduction of the Ketone Pendent Groups into Hydroxyl Groups. We have previously reported that ethylene ketal pendent groups in poly(ϵ-CL-*co*-TOSUO) copolymers can be completely deacetalized with formation of ketone pendent groups. These ketone groups have also been quantitatively reduced into hydroxyl pendent groups without scission of the polyester backbone.[27,32] These experimental conditions have been successfully used for the treatment of block copolymers of ϵ-CL and TOSUO (eq 5). Indeed, the ¹H-NMR analysis has confirmed that the extent of deacetalization is 100% and that the ketone groups are completely reduced to hydroxyl groups by sodium borohydride (see Figure 9a–c).



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SEC analysis has emphasized that deacetalization and reduction have no significant effect on the molecular weight distribution of the original poly(ϵ-CL-*b*-TOSUO) copolymer. For example, the molecular weight distribution of diblock copolymer (M_n(PCL)/M_n(PTOSUO) = 2900/2000) is originally 1.20, then 1.15 after deacetalization, and 1.10 after reduction as shown in Figure 11. The elution time slightly increased upon the conversion of the ethylene ketal pendent groups into ketones and then into hydroxyl groups. This indicates that some chain contraction occurs in THF when the polarity of the pendent groups is increased. All in all, there is a good consistency between ¹H-NMR and SEC analysis.

Thermal Analysis. (1) DSC Analysis of Poly(TOSUO) and Block Copolymers. Thermal transi-

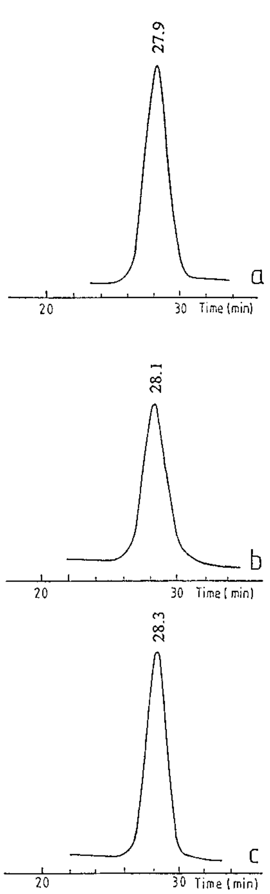

Figure 11. SEC chromatograms of poly(ϵ-CL-*b*-TOSUO) copolymer (M_n = 2900/2000): (a) before deacetalization; (b) after deacetalization; (c) after reduction.

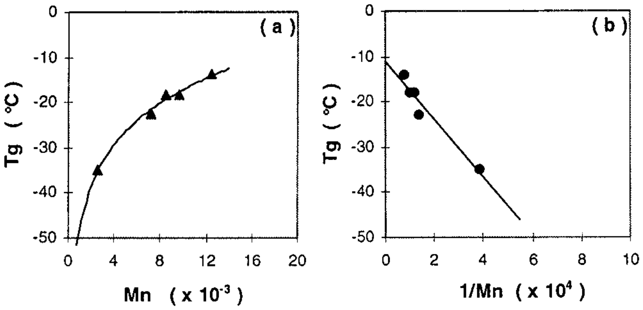

Figure 12. Dependence of T_g of poly(TOSUO) on molecular weight.

tions of PTOSUO and block copolymers have been analyzed by differential scanning calorimetry (DSC). The glass transition temperature (T_g) of PTOSUO depends on molecular weight. The expected dependence of T_g on M_n is illustrated in Figure 12a, in agreement with the commonly accepted eq 6, where T_g^{∞} is T_g for

$$T_g = T_g^{\infty} - K/M_n \qquad (6)$$

an infinite number average molecular weight (M_n) and K is a constant for the polymer under consideration. Indeed, a linear relationship is observed when the reciprocal number average molecular weight ($1/M_n$) is plotted as a function of T_g (Figure 12b). Thus, from the shift and slope of the straight line, T_g^{∞} and K can be estimated at −11 °C and 6.4 × 10^4, respectively.

Table 2. DSC Data for Poly(TOSUO), Poly(ϵ-CL-b-TOSUO), and Poly(ϵ-CL-*b*-TOSUO-b-ϵ-CL)

samples	M_n ($\times 10^{-3}$)	T_g (°C)	T_m (°C)	ΔH_m (J/g)
PTOSUO	2.6	−35		
PTOSUO	7.2	−23	49	22.3
PTOSUO	8.4	−18	53	42.9
PTOSUO	9.6	−18	52	41.2
PTOSUO	12.4	−14	52	35.0
PTOSUO/PCL	12.4/14.8	−47, −15	60	50.8 (111.4[a])
PCL	2.9	−61	58	135.2
PCL/PTOSUO	2.9/2.0	−46, −36	55	68.5 (115.7[a])
PCL/PTOSUO/PCL	2.9/2.0/1.0	−49, −39	57	73.1 (110.6[a])

[a] Calculated with respect to PCL content.

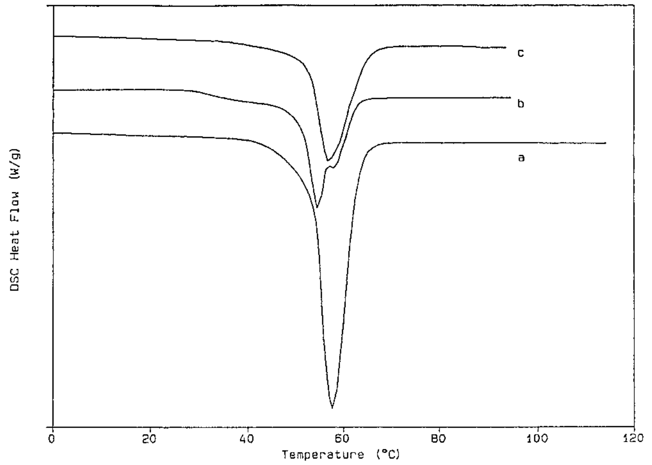

Figure 13. DSC thermograms (first scan) of (a) PCL (M_n = 2900), (b) diblock copolymer PCL/PTOSUO (M_n = 2900/2000), and (c) triblock copolymer PCL/PTOSUO/PCL (M_n = 2900/2000/1000).

DSC analysis of block copolymers (Table 2) shows two glass transitions, in agreement with a two-phase morphology. T_g of each polyester block is however different than T_g for the parent homopolymer (higher for PCL and smaller for PTOSUO). The observation that T_g's of the constitutive blocks are shifted to each other is indicative of a partial miscibility of the amorphous PCL and PTOSUO phases, at least in the range of molecular weight and composition under consideration.

It is worth mentioning that the melting endotherm of PTOSUO, which has previously been precipitated from a heptane solution, is only observed for the first scan. No melting peak is indeed observed even when the sample is cooled from the melt down to −100 °C at a rate lower than 2 °C/min and after annealing at ambient conditions for 1 week. Table 2 lists DSC data. The melting temperature and melting enthalpy of PTOSUO are lower compared to those of PCL. When the molecular weight of PTOSUO is too low (i.e., 2.6 × 10^3), no melting endotherm can be observed. Block copolyesters show an asymmetric melting endotherm (Figure 13 b,c), which might reflect that the PCL crystallization is perturbed by the PTOSUO immiscible component, resulting in decreased melting temperature and melting enthalpy (see Table 2). When a third PCL block is added to the poly(ϵ-CL-*b*-TOSUO) diblock copolyester, this effect is less dramatic as a result of an increased PCL percentage. The melting temperature and melting enthalpy of the triblock poly(ϵ-CL-*b*-TOSUO-*b*-ϵ-CL) copolyester are lower compared to those of homoPCL, but slightly higher than for the diblock poly(ϵ-CL-*b*-TOSUO) copolyester.

Table 3 illustrates how the thermal properties of the poly(ϵ-CL-*b*-TOSUO) changes upon the chemical modification of the pendent groups. Ketone substituents are responsible for some increase in T_g and T_m, although

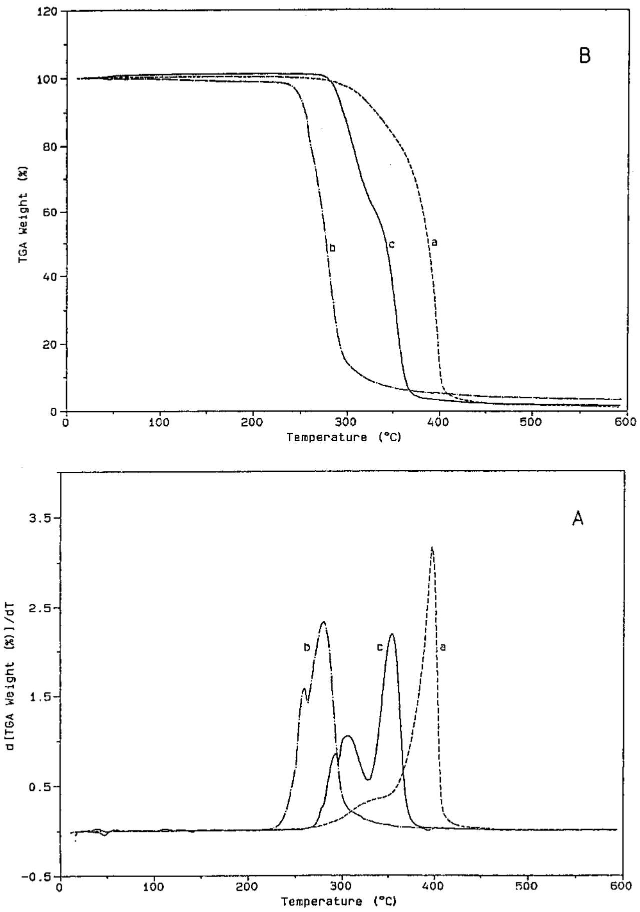

Figure 14. TGA curves for homopolyesters and block copolyester: (a) PCL (M_n = 10000); (b) PTOSUO(M_n = 12400); (c) poly(TOSUO-*b*-ϵ-CL) (M_n = 12400/14800).

Table 3. Effect of Chemical Modification of Poly(TOSUO) Block on the Thermal Properties of Poly(ϵ-CL-*b*-TOSUO) Diblock Copolymers

samples	pendent group	M_n ($\times 10^{-3}$)	T_g (°C)	T_m (°C)	ΔH_m (J/g)
PCL/PTOSUO	ethylene acetal	2.9/2.0	−46, −36	55	68.5
PCL/PTOSUO-K	ketone	2.9/1.4	−42, −26	59	55.5
PCL/PTOSUO-H	hydroxyl	2.9/1.4	−44, −22	60	120.7

the melting enthalpy becomes smaller. Substitution of hydroxyl for the ketone groups results in a further increase in T_g, T_m, and particularly ΔH_m. It thus appears that the PCL crystallization is dramatically enhanced by the hydroxyl groups of the polyester partner.

(2) Thermogravimetric Analysis of the Homopolyesters and Block Copolyesters. The thermogravimetric analysis shows that PCL and PTOSUO experience a sharp thermal decomposition with an inflection temperature at 397 and 279 °C, respectively (Figure 14B). Obviously, PTOSUO is less stable than PCL, whereas an intermediate thermal stability is observed for the block copolyester. Furthermore, the derivative-temperature curves (Figure 14A) clearly show a two-stage thermal degradation for the block copolyester at 306 and 320 °C (peak maximum temperature), which correspond to degradation of the PTOSUO block and the PCL block, respectively.

Conclusions

Homopolymerization of 1,4,8-trioxa[4.6]spiro-9-undecanone (TOSUO) initiated with aluminum isopropoxide in toluene at 25 °C yields a polymer of a predictable molecular weight and a narrow molecular weight distribution. Polymerization proceeds through a coordination–insertion mechanism with selective cleavage of the acyl-oxygen bond of the monomer. Kinetics is first order with respect to both the monomer and the initiator, with an absolute rate constant of 21 L·mol^{-1}·min^{-1}. Block copolymers have successfully been synthesized in toluene at 25 °C with aluminum isopropoxide as an initiator. Monomers A (ϵ-CL) and B (TOSUO) have sequentially been polymerized, so that AB, BA, and ABA block copolymers have been prepared. ^{13}C-NMR and SEC analysis have confirmed the absence of side reactions and the actual formation of the expected block copolymers. Conversion of the ethylene ketal pendent groups of the PTOSUO block to ketones and reduction of these ketones into hydroxyl groups have also been completely carried out without any scission of the polyester backbone. Thus the extent of both deacetalization of PTOSUO and reduction of the formed ketones can be as high as 100%. Interestingly, PTOSUO easily provides alternative structures for PCL, since the central methylene group of the PCL repeat units can be substituted by an ethylene ketal group (PTOSUO), replaced by a ketone (deacetalized PTOSUO), or substituted by a hydroxyl group (deacetalized PTOSUO + reduction). This flexibility in the polyester structure is expected to have great potential in the medical field.

The glass transition temperature of PTOSUO is higher than that of PCL, in contrast to the melting temperature, which is higher for PCL. However, the crystallization rate of PTOSUO in the melt is so slow that an amorphous material is commonly formed. Block copolymers of PTOSUO and PCL show the glass transition of each constitutive component. Crystallization of PCL is clearly influenced by the PTOSUO component and its alternative structures.

PTOSUO homopolymer is thermally less stable than PCL, whereas an intermediate thermal stability is observed for the diblock copolymers.

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