Synthesis of Eight- and Star-Shaped Poly(ε-caprolactone)s and Their Amphiphilic Derivatives

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Abstract: Spirocyclic tin dialkoxides are unique initiators for the ring-expansion polymerization of lactones leading to complex, but well-defined macromolecular architectures. In a first example, ε-caprolactone (εCL) was polymerized, followed by the resumption of polymerization of a mixture of εCL and εCL α-substituted by a chloride (αClεCL), so leading to "living" eight-shaped chains. Upon hydrolysis of the alkoxides, a four-arm star-shaped copolyester was formed, whose each arm was grafted by conversion of the chloride units into azides, followed by the Huisgen's [3+2] cycloaddition of alkyne end-capped poly(ethylene oxide) (PEO) onto the azide substituents. The complexity of this novel amphiphilic architecture was increased further by substituting the four-arm interconnecting PCL by an eight-shaped PCL. In a preliminary step, εCL was polymerized followed by a few units of εCL α-substituted by an acrylate. The intramolecular photo-crosslinking of the acrylates adjacent to the tin dialkoxides was effective in stabilizing the eight-shaped polyester while preserving the chain growth sites. This quite unusual tetrafunctional macroinitiator was used to copolymerize εCL and αClεCL, followed by hydrolysis of the alkoxides, conversion of the chloride units into azides and grafting of the four arms by PEO (see above). This architecture reported for the very first time is nothing but a symmetrical four-tail eight-shaped copolyester macromolecule.

Keywords: click chemistry · macrocycles · macromolecular engineering · polymerization · ring-expansion polymerization

Introduction

Nowadays, huge effort is devoted to the synthesis of increasingly more complex macromolecular architectures, including comb-, star- and ring-shaped polymers and their grafted versions. The interest for star-shaped polymers has to be found in unique physical properties compared with their linear counterparts.[1] The "core-first" and the "arm-first" methods were reported for the synthesis of star-shaped (co)polyesters.[2] Kricheldorf et al.[3] prepared in 2002 a four-arm star-shaped poly(oxepan-2-one) [poly(ε-caprolactone) or PCL] **3** by initiating the ring-expansion polymerization of oxepan-2-

one (ε-caprolactone or εCL) by spirocyclic tin(IV) alkoxide **1**, followed by hydrolysis (or acylation) of the chain growing centers of **2** (Scheme 1). This strategy was extended to the polymerization of other monomers, such as 3,6-dimethyl-1,4-dioxane-2,5-dione (lactide or LA), in order to make the corresponding star-shaped polyesters available.[3,4]

Ring-shaped polymers received much less attention, more likely because tedious strategy had to be worked out.[2] Nevertheless, polydispersed macrocycles can be formed by kinetically controlled step-growth polymerization.[5] Well-defined macrocycles can also be synthesized by direct coupling of the two chain-ends of linear precursors under very high dilution ($<10^{-5}$ M).[2,6] The limitation of this method is that, whenever the molecular weight of the precursor is too high, the direct coupling is quite a problem because of coupling is then much less probable than the undesired chain extension.[6] Very recently, an original process was reported for the synthesis of high molecular weight (20000) cyclic PCL. The synthetic strategy relies on the sequential polymerization of εCL and a few units of 1-(2-oxooxepan-3-yl)ethyl acrylate (αAεCL) (15–20) initiated by 2,2-dibutyl-2-stanna-1,3-dioxepane (DSDOP) with formation of tin-containing

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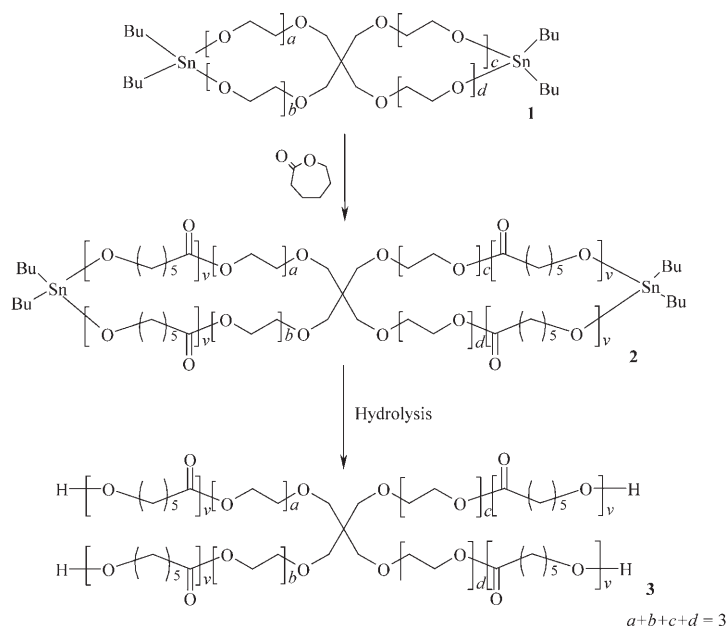
Scheme 1. Synthesis of star-shaped PCL.

macrocycles, followed by the intramolecular photo-cross-linking of the acrylates under moderate dilution ($\approx 10^{-4}$ M), and the final hydrolysis of tin alkoxides[7] (Scheme 2). Remarkably, tin alkoxides were untouched by photo-cross-linking, and the ring-expansion polymerization of εCL and L-LA could be resumed for making tadpole-shaped copolyesters with either two PCL[7] or two poly(L-LA)[8] tails available. Amphiphilic sun-shaped cyclic PCL-*graft*-PEO copolymers were also synthesized by grafting ω-carboxyl-PEO onto cyclic PCL substituted by hydroxyl groups.[9]

Last but not least, few approaches were reported in the scientific literature for the synthesis of eight-shaped polymers. Eight-shaped polystyrene[10] and polyisoprene[11] were synthesized by coupling of living α,ω-dianionic chains by tetrachlorosilane with a 2:1 chain/Si molar ratio under high dilution. Another route was based on the intramolecular cyclization of the two arms of a tadpole-shaped poly(isoprene),
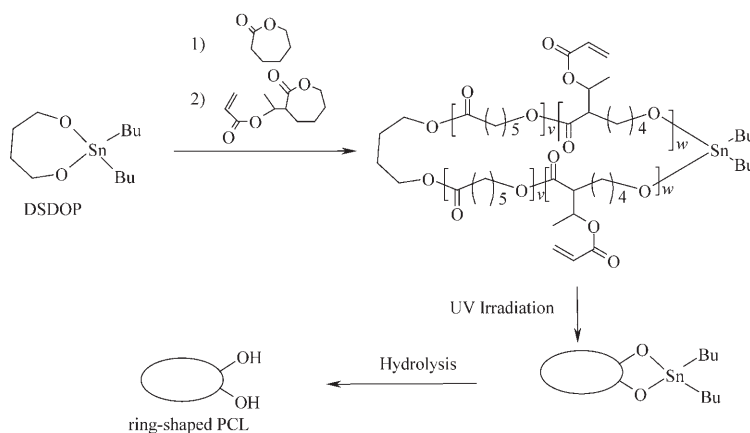
whose the end-group was a carbanionic species, the coupling agent being (CH$_3$)$_2$SiCl$_2$.[12] Eight-shaped poly(chloroethyl vinyl ether)s (PCEVE) were also synthesized by the intramolecular cyclization of tetrafunctional linear precursors, that is, α,α′-distyrenyl-ω,ω′-diacetal-poly(CEVE), catalyzed by a Lewis acid (SnCl$_4$) as catalyst.[13] In an alternative approach, endocyclic amino group of macrocyclic polystyrene was reacted with a difunctional reagent (glutaric acid) with formation of bicyclic polystyrene.[14] Tezuka et al. reported the synthesis of eight-shaped poly(THF) based on a pre-cyclization step by electrostatic interactions, that were ultimately substituted by covalent bonds.[15,16] All these processes have two major drawbacks. Indeed, they need high dilution, and the synthesis of high molecular weight eight-shaped polymers is challenging.

Parallel to their cyclization, aliphatic polyesters were grafted by reactive/functional groups in order to broaden the range of their properties and applications.[17] In this respect, a "click" reaction, that is, the Huisgen's [3+2] cycloaddition of alkynes and azides was very promising.[18–21] This copper-catalyzed reaction was quantitative under very mild conditions, and tolerated several functional groups thus avoiding cumbersome protection/deprotection steps. Remarkably, no chain degradation occurred when the reaction was carried out in an organic solvent (THF, DMF) at low temperature (35°C).[22,23] An additional advantage of the Huisgen's cycloaddition may be found in the inertness of the formed triazole ring towards metabolic transformation. For instance, Emrick et al. showed that PCL-*graft*-PEO, prepared by this "click" chemistry, was not cytotoxic for L929 mouse fibroblasts.[24] This reaction is thus well-suited for the modification of biodegradable and biocompatible aliphatic polyesters with potential biomedical applications. Recently, star-shaped copolymers were synthesized by "click" chemistry according to the "arm-first" approach.[25–27]
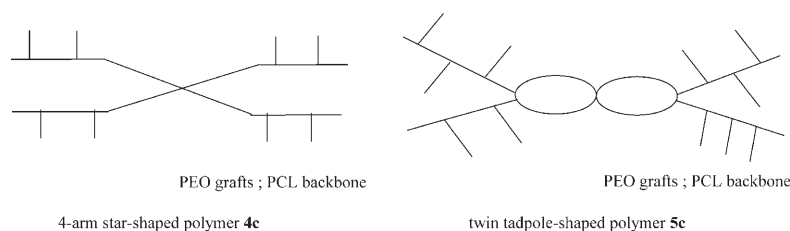
The aim of this paper is to go a step further in the macromolecular engineering of PCL by combining judiciously ring-expansion polymerization and "click" chemistry. Two novel architectures were targeted, that is, a four-arm star-shaped polyester **4c**, whose each arm is a PCL-*block*-(PCL-*graft*-PEO) copolymer [where PEO stands for poly(ethylene oxide)], and the same architecture where the four arms interconnecting PCL are substituted by an eight-shaped PCL (**5c**). These architectures are shown in Scheme 3.

Results and Discussion

Synthesis of star-shaped diblock copolyesters 4a: The general strategy for the synthesis of star-shaped copolyesters relies on the sequential polymeri-

Scheme 2. Synthesis of ring-shaped PCL.

PEO grafts ; PCL backbone

PEO grafts ; PCL backbone

4-arm star-shaped polymer **4c**

twin tadpole-shaped polymer **5c**

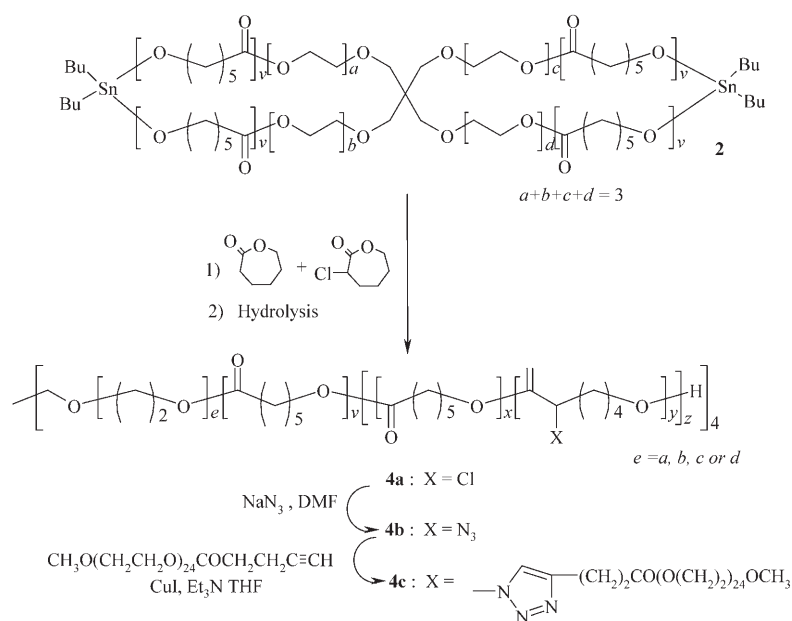Scheme 3. Star- and eight-shaped copolymers with a tadpole substructure.

zation of εCL followed by a mixture of εCL and 3-chlorooxepan-2-one (α-chloro-ε-caprolactone or αClεCL) initiated by a spirocyclic tin(IV) alkoxide **1**.[3] After hydrolysis of the propagating alkoxides, the activated chlorides are derivatized into azides, which added alkyne end-capped PEO via a cycloaddition reaction.[17,22,30]

This synthetic route takes advantage of two previous contributions, that is, controlled ring-expansion copolymerization of αClεCL and εCL initiated by cyclic tin(IV) alkoxides,[29] and synthesis by Kricheldorf et al. of a soluble spirocyclic tin initiator **1** by condensation of the hydroxyethylated pentaerythritol (Mn, ≈270) with 2 equiv of dibutyl tin(IV) dimethoxide (Bu$_2$Sn(OMe)$_2$) in hot toluene.[28] This spirocyclic tin alkoxide **1** is actually able to initiate the ring-expansion polymerization of lactones and lactide with formation of four-arm star-shaped polyesters.[3] In this work, a four-arm star-shaped diblock copolyester, 4-*star*-poly(εCL-b-(εCL-co-αClεCL)) **4a**, was prepared by initiating the polymerization of εCL by the spirocyclic tin alkoxide **1** at 40°C (Scheme 1). After 2 h, a sample was taken for analysis. The degree of polymerization determined by ^{1}H NMR (DP$_{NMR,εCL}$=363) fully agreed with the theoretical value (DP$_{th,εCL}$=360). Then, a freshly prepared mixture of εCL and αClεCL was transferred to the polymerization medium (Scheme 4). Two hours later, the propagating tin alkoxides were hydrolyzed and the star-shaped diblock copolyester **4a** was precipitated in cold heptane and collected by filtration. The average polymerization degree of εCL and αClεCL in the second block was 266 and 166, respectively, as calculated from the integration of the ^{1}H NMR signals at δ 4.25 ppm for αClεCL and at 2.25 ppm for εCL, in agreement with the theoretical values (DP$_{th,εCL}$=270, DP$_{th,αClεCL}$=170). The total molecular weight of the star-shaped copolyester **4a** was thus 97.0×10^3, the SEC trace was symmetrical and the polydispersity index was 1.45 quite
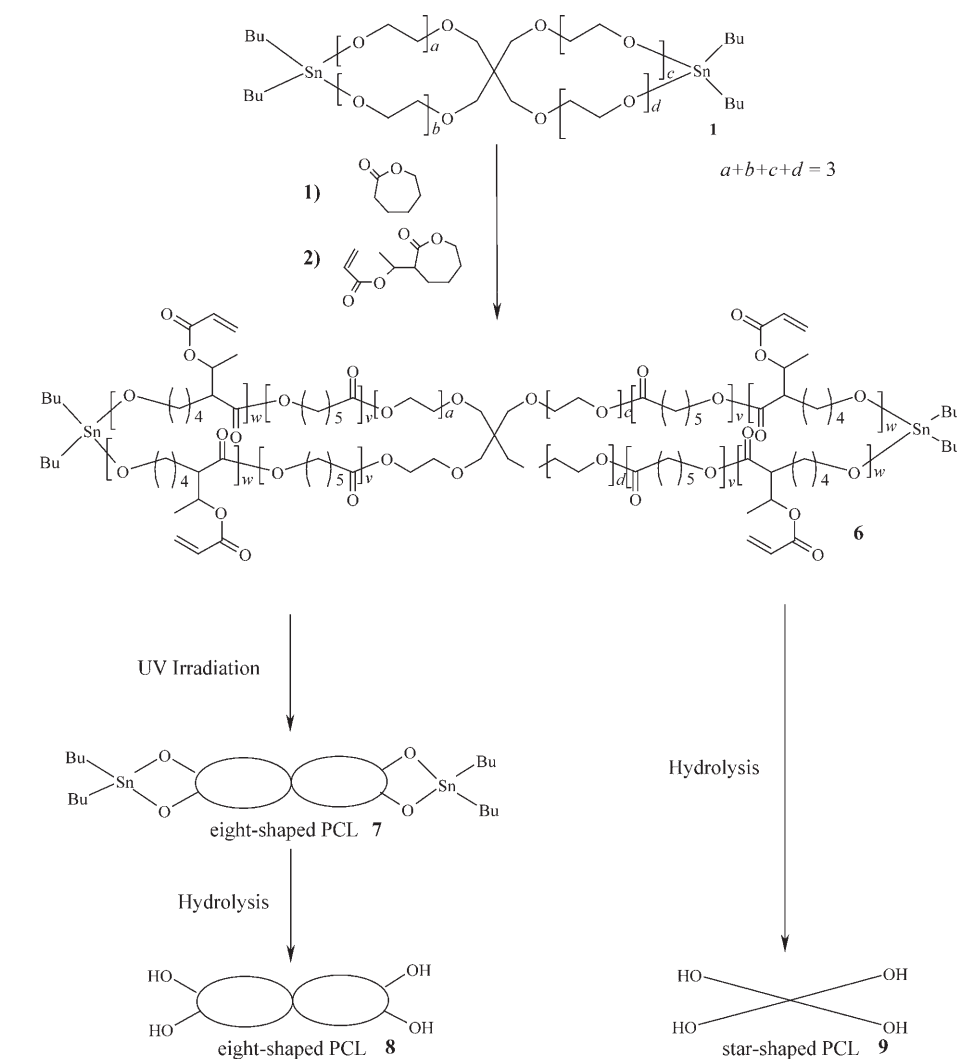
consistent with the previously published results by Kricheldorf et al.[28]

Synthesis of eight-shaped macrocyclic poly(ε-caprolactone): High molecular weight eight-shaped PCL was synthesized as an extension of the strategy mentioned in the introduction and illustrated in Scheme 2.
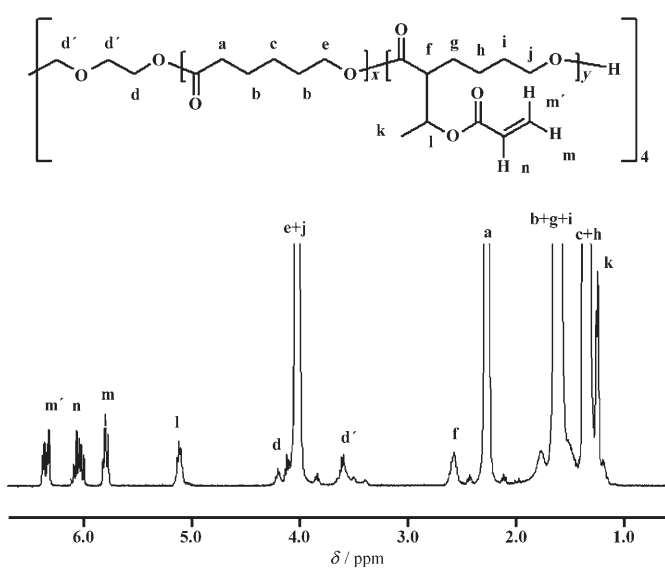
Because this strategy does not require high dilution and is not restricted to small rings, it is more appropriate for going a step further in the complexity of the eight-shaped architecture. First, the polymerization of εCL was initiated in toluene by the spirocyclic tin initiator **1** at 40°C for 2 h, the monomer conversion being close to completeness as assessed by ^{1}H NMR analysis (Scheme 5). Then, a fresh solution of αAεCL was added to the polymerization medium in order to form a short block with pendant unsaturated groups. After 2 h at 60°C, a sample was withdrawn, and **6** was hydrolyzed into the parent star-shaped copolyester **9** for characterization (Scheme 5). The ^{1}H NMR spectrum (Figure 1) of the copolyester **9** shows a set of resonances at δ 6.4 ppm, 6.1 ppm and 5.8 ppm, typical of the protons of the αAεCL units. The average polymerization degree of αAεCL (DP$_{αAεCL}$=36.7) was calculated from the integration of the ^{1}H NMR signals at 6.4 ppm for the αAεCL units and at 2.25 ppm for the εCL units, which is close to the theoretical value of 40, thus to the complete conversion of the second comonomer. The SEC trace (Figure 2) was symmetrical, and the polydispersity index (1.45) was comparable to values reported for polylactones prepared with the initiator **1**.[28] M_n (29×10^3) determined by SEC with an universal calibration,

$a+b+c+d = 3$

1)

2) Hydrolysis

4a : X = Cl

4b : X = N$_3$

4c : X =

NaN$_3$, DMF

CH$_3$O(CH$_2$CH$_2$O)$_{24}$COCH$_2$CH$_2$C≡CH
CuI, Et$_3$N THF

e =a, b, c or d

—(CH$_2$)$_2$CO(O(CH$_2$)$_2$)$_{24}$OCH$_3$

Scheme 4. Synthesis of star-shaped copolymers, whose the 4 arms are grafted.

a+b+c+d = 3

1)

2)

UV Irradiation

eight-shaped PCL 7

Hydrolysis

eight-shaped PCL 8

Hydrolysis

star-shaped PCL 9

Scheme 5. Synthesis of eight-shaped copolymers.

was lower than $M_{n,NMR}$ of 42.6×10^3, at least partly because star-shaped PCL has a smaller hydrodynamic volume than linear PCL of the same molecular weight.[1] The spiro-macrocyclic precursor 6 was diluted with dry toluene (≈ 0.5 wt%) and irradiated by UV (350–420, 1000 W) at room temperature for 120 min in the presence of 1 mol% of benzophenone with respect to the acrylic units. ^{1}H NMR analysis showed that the average number of unsaturated acrylic units decreased from 36.7 to 14.7, as result of the expected cross-linking reaction. Figure 2 compares the SEC traces for the hydrolyzed sample before and after UV treatment. The apparent $M_{n,SEC}$ decreased from 29.0×10^3 to 24.0×10^3 upon cross-linking, merely because of the successful conversion of linear into cyclic macromolecules.[6] This is an essential observation that confirms that the ring-shape of the copolyester 8 is maintained after hydrolysis of the endocyclic tin alkoxides of 7. The SEC trace was symmetrical and unimodal after hydrolysis, and the cyclization reaction did not change the molar mass distribution ($M_w/M_n = 1.45$), which is evidence for the well-controlled

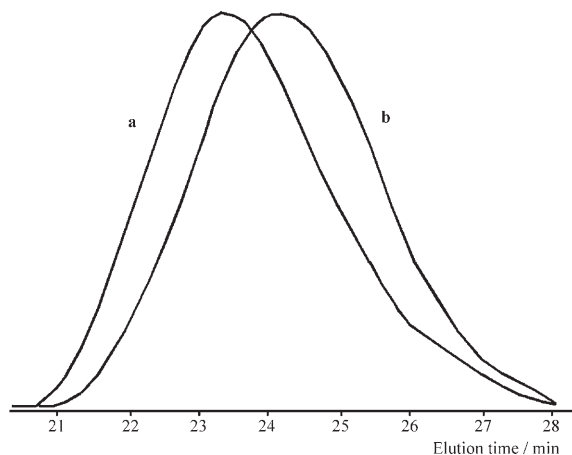Figure 1. ^{1}H NMR spectra star-shaped copolyester.

Figure 2. SEC traces for the a) star-shaped PCL and b) eight-shaped PCL after hydrolysis of the propagating tin alkoxides.

formation of eight-shaped macrocycles. The ratio of the molecular weights at the maximum of the elution peaks [$M_{p,SEC}$(cyclic)/$M_{p,SEC}$(linear)] was 0.65, then smaller than the value (0.76) previously reported for monocyclic PCL ($M_n = 24.0 \times 10^3$)[7] and in agreement with data published for other bicyclic polymers.[14]

In parallel, a blank experiment was carried out in order to prove the absence of any degradation during the UV treatment. Polymerization of εCL (9 mmol) was initiated by the spirocyclic tin alkoxide 1 (0.025 mmol) at 40°C for 2 h. A sample was picked out and hydrolyzed into four-arm starshaped PCL for characterization. Then, the polymerization medium was UV irradiated under the conditions used for cyclization. The SEC traces before and after UV treatment could be superimposed and the polydispersity (1.45) was unchanged, which supports that the polyester chains are stable under UV irradiation.

Synthesis of eight shaped copolyesters 5a attached with four chlorinated tails: It was previously reported that not only the copolyester chains but also the propagating tin alkoxides resisted the UV treatment. Therefore, the bicyclic copolyesters are typical macroinitiators able to resume the ring-expansion polymerization of a mixture of εCL and αClεCL and to impart a tadpole structure to the individual macrocycles.[7,8,30] After UV irradiation, the spiro-macrocyclic PCL precursor 7 (Scheme 5) was concentrated and then added with a solution of εCL and αClεCL in dry toluene (Scheme 6). The polymerization mixture was stirred at 40°C for 2 h. The resumption of the εCL and αClεCL copolymerization into 5a was confirmed by ¹H NMR spectrum (Figure 3). Indeed, new resonances were detected at 4.25 ppm (-COCHCl-), 4.15 ppm (-CH₂O-) and 2.0 ppm (-CHClCH₂-) typical of the protons for the αClεCL units. Moreover, the relative intensity of the signals at 4.0, 2.25, 1.6 and 1.4 ppm typical of the protons for the εCL units increased significantly. The average polymerization degrees of εCL and αClεCL in the four tails of the

bicyclic chains were 246 and 190, respectively, as calculated from the integration of the ¹H NMR signals at 4.25 ppm for αClεCL and 2.25 ppm for εCL, in good agreement with the theoretical values ($DP_{th,εCL} = 250$, $DP_{th,αClεCL} = 186$). The SEC trace of the derivative 5a (Scheme 6) was shifted towards shorter elution times, while keeping the polydispersity index unchanged ($M_w/M_n = 1.50$). The apparent molecular weight was actually increased ($M_{n,SEC} = 34.8 \times 10^3$), compared to the spirocyclic PCL ($M_{n,SEC} = 24.0 \times 10^3$, $M_w/M_n = 1.45$). It can, thus, be concluded that the polymerization resumption was effective. To the best of our knowledge, this is the first example of an eight-shaped architecture substituted at the same place by two dangling chains.
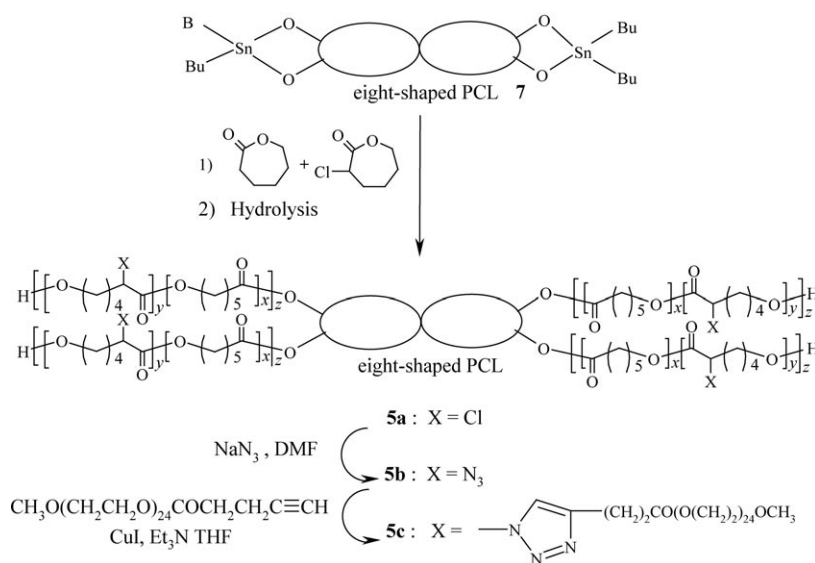
Scheme 6. Synthesis of eight-shaped copolymers with a tadpole substructure.
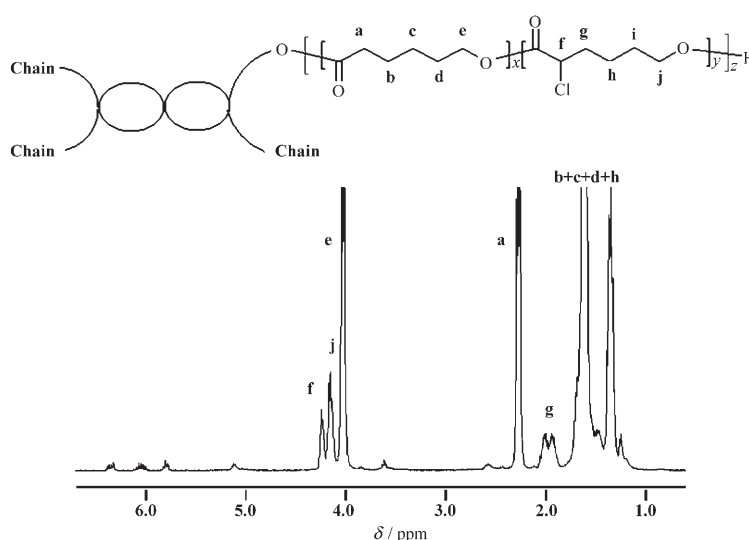

Figure 3. ¹H NMR spectrum for the four-tail eight-shaped PCL with chlorinated tails, 5a.

Synthesis of star- and eight-shaped copolyesters, 4b and 5b, with azide containing tails: Riva et al. previously reported that the chloride substituents of linear poly(αClεCL-*co*-εCL) copolymers were quantitatively converted into azides by reaction with sodium azide, under non-degrading conditions for the polyester chains, that is, in DMF at room temperature overnight.[22] Therefore, the pendant chloride groups of the chlorinated star- and eight-shaped copolyesters **4a** and **5a** herein prepared, were converted into azides under the same conditions (Schemes 4 and 6). A strong IR absorption characteristic of the azide groups was observed at 2107 cm⁻¹ (not shown). The ¹H NMR spectrum for the derivative **5b** (Scheme 6) is shown in Figure 4. Upon substitution of azide for chloride, the signal at 4.1 ppm assigned to the -CH_2OCO(Cl)CH- protons was slightly shifted downfield to 4.2 ppm for the -CH_2OCOCH(N$_3$)- protons. The resonances at 4.25 and 2.0 ppm, assigned to the -COCHCl- and the -CH_2OCO(Cl)CH- protons of the αClεCL units, respectively, disappeared completely, and a new resonance at 3.8 ppm, assigned to the -COCHN$_3$- proton typical of the αN$_3$εCL units, was observed, which supported the completeness of the derivatization reaction. The same observation was reported for the conversion of the star-shaped diblock copolyesters **4a** into **4b**. Moreover, the azide content of the tails in **5b** (F$_{αN3εCL}$=0.43) and in the second blocks in **4b** (F$_{αN3εCL}$=0.38) was determined by ¹H NMR analysis and was in good agreement with the composition of the precursors **5a** (F$_{αClεCL}$=0.43) and **4a** (F$_{αClεCL}$= 0.38). Finally, the SEC traces (not shown) before and after the substitution reaction could be superimposed, as expected for non degrading reaction conditions.

Grafting of α-alkyne PEO onto the azide-containing star- and eight-shaped derivatives, 4b and 5b, by "click" chemistry: α-Alkyne PEO was grafted onto the pendant azides of the arms of the star-shaped polyester **4b** and the tails of the eight-shaped polyester **5b** under the

conditions reported by Riva et al. (Schemes 4 and 6).[8,22,23,30] The copolyesters **4b** and **5b** were reacted with 1.0 equiv (with respect to the αN$_3$εCL units) of alkynyl end-capped PEO, in THF in the presence of CuI and triethylamine at 35°C. The reaction was monitored by FTIR spectroscopy. After 4 h, a significant decrease of the stretching frequency at 2107 cm⁻¹, typical of the azide groups, and the appearance of an absorption at 1646 cm⁻¹, typical of the triazole ring, showed that the Huisgen's cycloaddition occurred as expected. The PEO-grafted copolymers **4c** and **5c** were precipitated in cold diethyl ether and the unreacted PEO was eliminated by repeating three times the precipitation. Figure 5 shows the ¹H NMR spectrum for the PEO-grafted
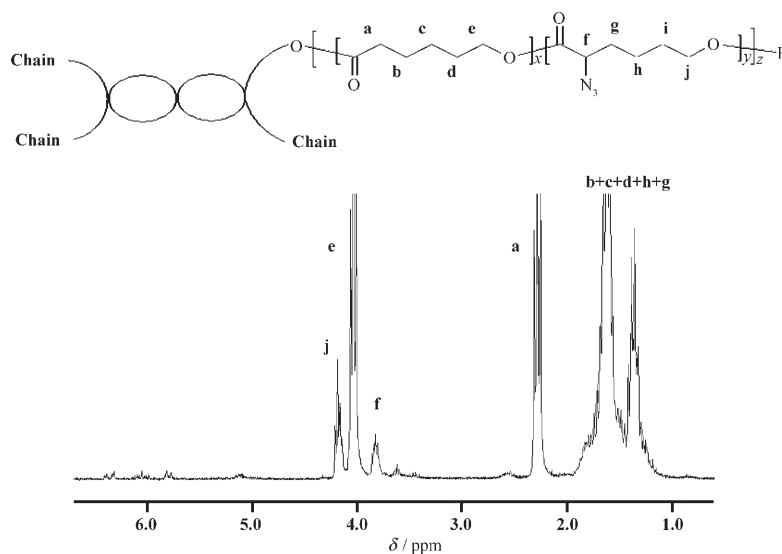

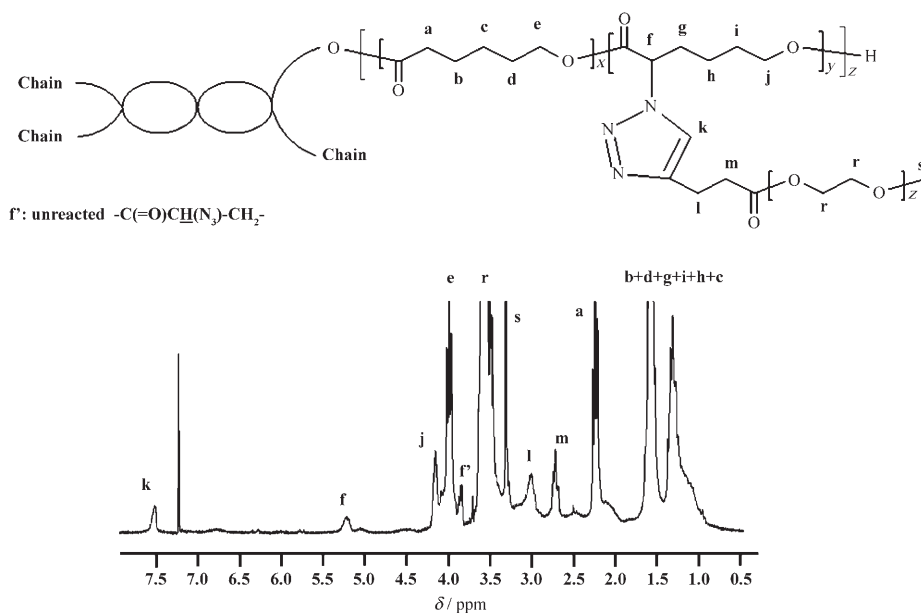Figure 4. ¹H NMR spectrum for the four-tail eight-shaped PCL with azide containing tails, **5b**.

Figure 5. ¹H NMR spectrum for the amphiphilic four-tail eight-shaped PCL, **5c**.

copolymer **5c**. A set of new peaks was clearly observed at i) 7.5 ppm (singlet) typical of the methine proton of the triazole ring, ii) 5.2 ppm assigned to the -COCH(1-triazole)-proton, iii) 3.6 ppm typical of the protons for the ethylene oxide units, iv) 3.3 ppm for the methoxy protons, v) 3.0 ppm for the -(4-triazole)-CH_2CH$_2$CO-(OCH$_2$CH$_2$)$_{24}$OCH$_3$ protons, and vi) 2.7 ppm for the -(4-triazole)-CH$_2$CH_2CO-(OCH$_2$CH$_2$)$_{24}$OCH$_3$ protons. The grafting efficiency (61%) was calculated from the relative intensity of the signals at 7.5 ppm for the triazole ring and at 2.25 ppm for the εCL units. Each tail of the copolymer **5c** was grafted by 29 PEO chains and M_n was 195×10^3 gmol^{-1} as determined by ^{1}H NMR. Similarly, each arm of the star-shaped copolymer **4c** was grafted by 16 PEO chains, and M_n was 150×10^3 gmol^{-1}. The reason for the lower grafting efficiency in the case of the star-shaped copolyester is not clear and hardly explained by the difference in the macromolecular architecture compared to the eight-shaped chains.

Figure 6 compares the SEC traces for the PEO-grafted copolymers **5c** and **4c**. Not only a lower molecular weight but also a more compact conformation can account for the higher elution time of the eight-shaped copolyester compared with the star-shaped chains. The polydispersity was slightly increased (from 1.50 to 1.75) as result of the PEO-grafting in line with the chromatograms that remained unimodal and symmetrical and with previously reported data.[17,30]
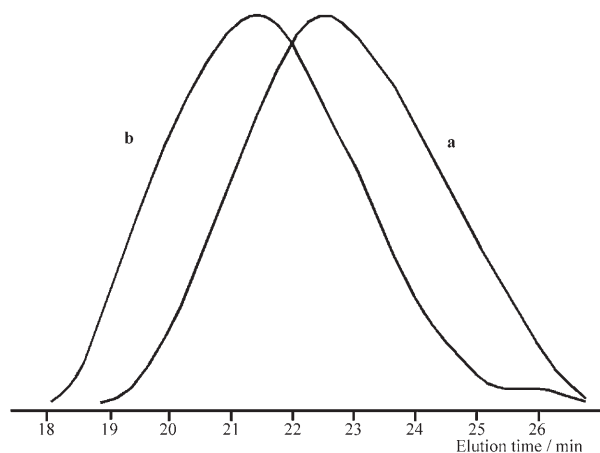

Figure 6. SEC traces for the PEO-grafted copolymers: a) **5c** and b) **4c**.

Figure 7. DSC traces during the cooling the run for a) star-shaped and b) eight-shaped PCL, after hydrolysis of the alkoxides.
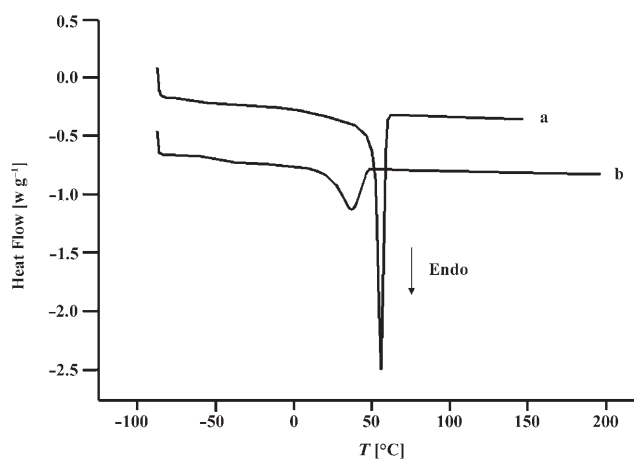
Figure 8. DSC traces during the second heating run for a) star-shaped and b) eight-shaped PCL, after hydrolysis of the alkoxides.

zation (**8**), and the melting temperature (T_m) decreased by 17°C (Table 1). In contrast, cyclization of PCL of high molecular weight had only a minor effect on T_g. The same evolution was previously observed for the impact of the cyclization of linear PCL on the thermal properties.[8]

It is worth noting that although crystallization of the eight-shaped PCL **8** manifested itself by one endotherm in the DSC trace (cooling from 120 to −90°C at a rate of 10°Cmin^{-1} (Figure 7), an equimolar mixture of the eight-shaped PCL **8** and the star-shaped PCL **9** exhibited two

Thermal properties: The thermal behavior of the star- and eight-shaped PCL **9** and **8** ($M_n = 41.2 \times 10^3$) (thus without chlorinated arm and tail, respectively) was compared by DSC (Figures 7 and 8). The crystallization enthalpy of the star-shaped PCL **9** decreased from 50.0 to 22.0% upon cycli-
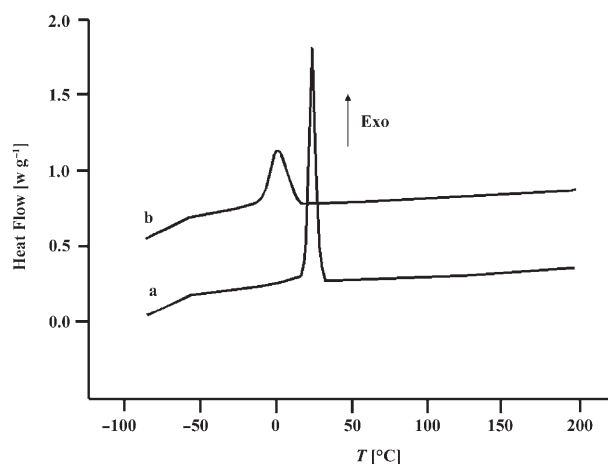
Table 1. Characteristic properties of star-shaped and eight-shaped PCL.

Samples	$M_{n,th}$ $\times 10^3$	$M_{n,NMR}$ $\times 10^3$	$M_{n,SEC}$[a] $\times 10^3$	M_w/M_n	T_g[b] [°C]	T_m[b] [°C]	ΔH_m[c] [Jg^{-1}]	T_c[b] [°C]	ΔH_c[c] [Jg^{-1}]	X_c[d] [Jg^{-1}]
eight-shaped PCL **8**	41.0	41.2	24.0	1.45	−52.5	37.5	30.0	0.5	28.5	22
star-shaped counterpart **9**	41.0	42.6	29.0	1.45	−56.0	54.5	67.5	23.5	52.5	50

[a] The experimental molecular weights were converted by the following equation: M_n(PCL) $= 0.259 \times M_n$(PS)$^{1.073}$ [b] T_g and T_m were measured during the second heating run at 10°Cmin^{-1} rate. T_c was measured during the cooling run after the first heating. [c] ΔH_m (ΔH_c) is the melting (crystallization) enthalpy measured under the same conditions as T_m (T_c). [d] $X_c = (\Delta H_m/\Delta H^0_{PCL}) \times 100$; $\Delta H^0_{PCL} = 136.4$ Jg^{-1}.[32]

crystallization peaks under the same conditions with a higher ΔH_c for the star-architecture (Figure 9). This observation gave credit to the efficiency of the photochemical ring closure, thus of conversion of **6** to **7** in Scheme 5.
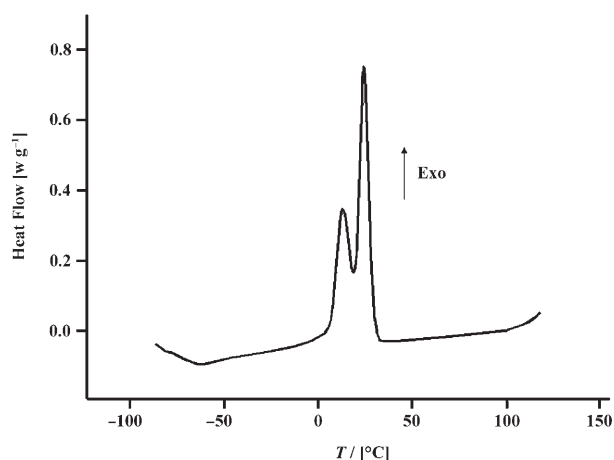

Figure 9. DSC trace monitored for the cooling of an equimolar mixture of star- and eight-shaped PCLs.

How the crystallization is influenced by the conversion of the chlorinated arms of the star-shaped PCL **4a** and the chlorinated tails of the eight-shaped PCL **5a** to the azide containing arms (**4b**) and tails (**5b**) and finally to the PEO grafted arms (**4c**) and tails (**5c**) on crystallization was also investigated by DSC (Figures 10 and 11). The copolymers were first heated to 120°C and then cooled down to −90°C at a rate of 10°Cmin⁻¹. The DSC traces during cooling are compared in Figure 10. A crystallization peak was clearly observed at 9.5°C for the chlorinated star-shaped diblock copolyester **4a** in contrast to a faint peak at a lower temper-
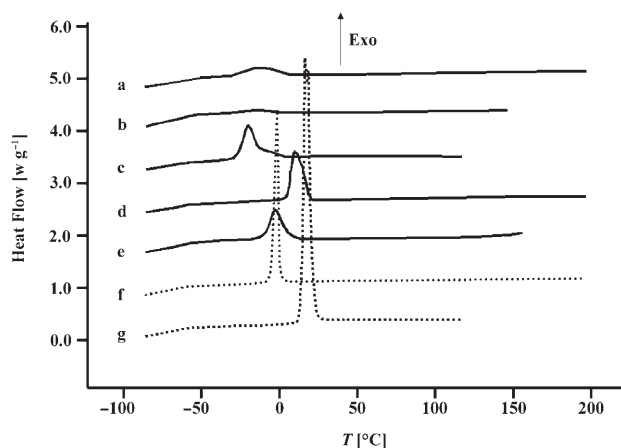

Figure 10. DSC traces during the cooling run for four-tail eight-shaped PCL a) with chlorinated tails, **5a**, b) with azide containing tails, **5b**; c) amphiphilic four-tail eight-shaped PCL, **5c**; d) four-arm diblock with a chlorinated block, **4a**; e) four-arm diblock with an azide containing block, **4b**; f) four-arm diblock with a PCL-g-PEO block **4c** and (g) linear homo-PEO.
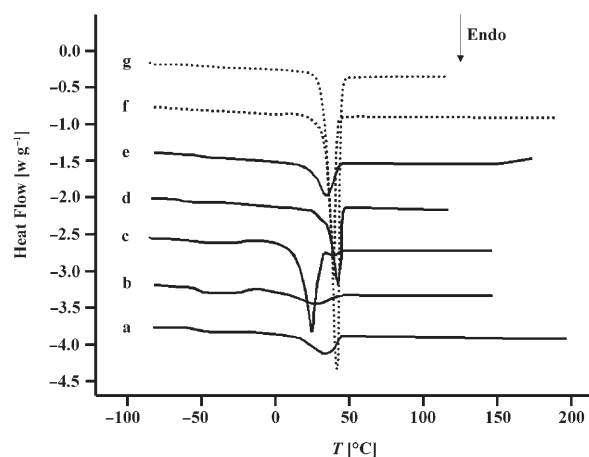

Figure 11. DSC traces during the second heating run for four-tail eight-shaped PCL a) with chlorinated tails, **5a**, b) with azide containing tails, **5b**; c) amphiphilic four-tail eight-shaped PCL, **5c**; d) four-arm diblock with a chlorinated block, **4a**; e) four-arm diblock with an azide containing block, **4b**; f) four-arm diblock with a PCL-g-PEO block **4c**; and g) linear homo-PEO.

ature (−13°C) for the chlorinated eight-shaped derivative **5a**. The crystallization enthalpy (ΔH_c) for **4a** (47 J g⁻¹) was much higher than that for **5a** (20.5 J g⁻¹), which means that the eight-shaped architecture is a severe restriction to the crystallization of PCL **5a**.

Moreover, comparison of data in Tables 1 and 2 shows that the crystallization temperature and enthalpy decreased by 12.5°C and 8 J g⁻¹, respectively, upon the grafting of four

Table 2. Physical properties of the derivatives from eight-shaped and star-shaped PCL.

Samples	T_g[a] [°C]	T_m[a] [°C]	ΔH_m[b] [J g⁻¹]	T_c[a] [°C]	ΔH_c[b] [J g⁻¹]
5a	−52.0	34.0	25.0	−13.0	20.5
5b	−53.5	27.5	14.0	−14.0	6.0
5c	−	25.5	56.0	−26.0	36.0
4a	−58.5	45.5	55.0	9.5	47.0
4b	−53.0	34.5	36.0	−2.7	35.0
4c	−	39.0	73.0	−1.5	64.5
homo-PEO (reference)	−	41.5	165.5	16.5	157.5

[a] T_g and T_m were measured during the second heating run at 10°Cmin⁻¹ rate. T_c was measured during the cooling run after the first heating. [b] ΔH_m (ΔH_c) is the melting (crystallization) enthalpy measured under the same conditions as T_m (T_c).

poly(αClεCl-*co*-εCL) tails onto the spirocyclic PCL. The same observation was reported when cyclic PCL was grafted by two semi-crystalline poly(L-lactide) tails[8] and by two amorphous poly(αClεCl-*co*-εCL) tails, respectively.[30] As a rule, the grafting of mono/spiro-cyclic PCL by two polymeric tails, amorphous or not, has a depressive effect on the crystallization of PCL.

Conversion of the chlorinated chains into the azide containing version decreased ΔH_c by 14.5 J g⁻¹ for spirocyclic

PCL (**5b** vs **5a**) and 12 J g⁻¹ for star-shaped PCL (**4b** vs **4a**). Crystallization of the PEO grafts was observed for the copolymers **4c** and **5c**, although at a much lower temperature and to a lesser extent than homo PEO. The large difference in ΔH_c (and T_c) between **4c** and **5c** is an additional evidence for the impact of the chain architecture.

All the samples were then heated from $-90\,°C$ at $10\,°C\,min^{-1}$, and the DSC traces were recorded as shown in Figure 11. The experimental data are listed in Table 2. Comparison of T_m and ΔH_m for the spirocyclic PCL (Table 1) and the samples **5a** and **5b** confirms the negative impact of the tails on the PCL crystallization to an extent that depends on the tail substituents, thus chlorides versus azides. The melting temperature of PCL was indeed decreased by $3.5\,°C$ in case of α-chlorides and by $10.0\,°C$ for the α-azide pendant groups. In parallel to T_m, the melting enthalpy for PCL was also decreased by $5.0\,J\,g^{-1}$ upon grafting of the chlorinated tails (**5a**) and by $16.0\,J\,g^{-1}$ when the tails contained azides rather than chlorides (**5b**). The melting temperature (T_m) and enthalpy (ΔH_m) for the chlorinated star-shaped diblock **4a** were significantly higher compared with the eight-shaped **5a**. A similar evolution was observed for the comparison of **4b** with **5b**, and **4c** with **5c**, respectively. Once again, there is a clear relationship between property and macromolecular architecture. When PEO was part of the copolymer, only this constitutive component crystallized, although with some restriction imposed by the complex architecture, as testified by a substantial decrease in T_m and ΔH_m compared with linear PEO (Table 2) and in agreement with the PEO-grafting of cyclic PCL.[30]
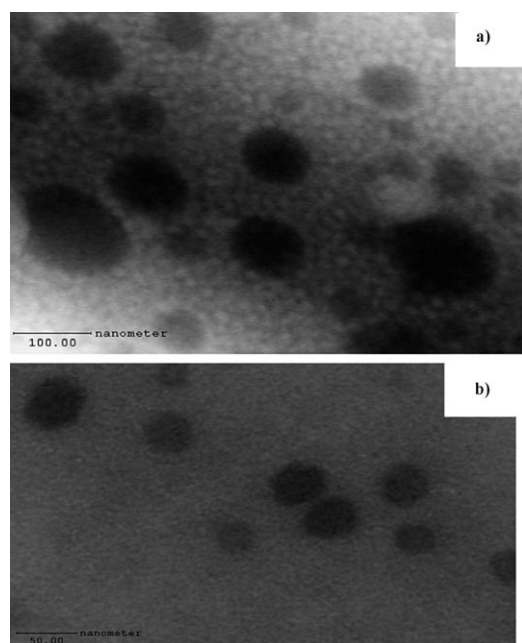

Figure 12. TEM of micelles of a) amphiphilic four-tail eight-shaped PCL, **5c** (scale bar 100 nm) and b) amphiphilic four-arm diblock, **4c** (scale bar 50 nm).

Micellization in water as result of the amphiphilicity and self-assembly of the grafted copolyesters **4c** and **5c** was an additional although qualitative evidence for the successful grafting of PEO onto the eight-shaped and star-shaped PCL, respectively. Ellipsoidal (for **5c**) and spherical (for **4c**) micelles were indeed observed by TEM (Figure 12), that are supposed to consist of a hydrophobic polyester core surrounded by a hydrophilic corona of PEO. The size of the micelles formed by the eight-shaped amphiphilic PCL/PEO copolymer was larger although it may not be concluded that the macromolecular architecture is responsible for this difference because the composition of **4c** and **5c** is not the same. In order to shed light on the impact of the architecture on the micellization of these amphiphilic PEO/PCL copolyesters in water, synthesis and characterization of a wider range of star- and eight-shaped PEO/PCL graft copolymers with different compositions are under current investigation.

Conclusion

This work reported on a successful strategy for the synthesis of novel functional star- and eight-shaped copolyesters. It relies on the combination of controlled ring-expansion polymerization of lactones initiated by a spirocyclic bis-tin(IV) dialkoxide, macrocyclization by the intramolecular photo-cross-linking of pendant unsaturations in the very close vicinity of the propagating sites, and "click" chemistry (Huisgen's [2+3] cycloaddition). As an example, an amphiphilic eight-shaped copolyester was synthesized; its constitutive macrocycles were grafted by two PCL-*graft*-PEO tails. To the best of our knowledge, this is the first example reported of a four-tail eight-shaped architecture with tails consisting of an amphiphilic graft copolymer. Model compounds can thus be synthesized for studying the micellization of amphiphilic star-shaped copolyesters but also eight-shaped copolyesters as such and with a tadpole substructure. In addition to micellization, self-assembly in the bulk deserves further investigation.

Experimental Section

Materials: εCL (Aldrich) was dried over calcium hydride at room temperature for 48 h and distilled under reduced pressure just before use. Spirocyclic tin alkoxide **1** was prepared according to Kricheldorf et al.[28] Synthesis of αAεCL,[8] αClεCL,[29] and alkynyl end-capped PEO[30] was reported elsewhere. Benzophenone (Aldrich) was purified by sublimation at 40 °C in vacuo and further dried by azeotropic distillation (three times) of toluene. Toluene (Aldrich, 99.5 %) was dried over a sodium/benzophenon complex and distilled under nitrogen. Dichloromethane was dried over calcium hydride and distilled under nitrogen before use. DMF (ACROS) was dried over P_2O_5 for five days and distilled under nitrogen before use. Poly(ethylene glycol) monomethyl ether ($M_n = 1050$) (PEO; Fluka), pent-4-ynoic acid (Aldrich), dicyclohexylcarbodiimide (DCC; Aldrich), 4-dimethylaminopyridine (DMAP; Fluka), sodium azide (Aldrich), diethyl ether, heptane and triethylamine (Aldrich) were used as received.

Characterization: Size-exclusion chromatography (SEC) was performed in THF at a flow rate of 1.0 mL min^{-1} at 40°C with a Hewlett-Packard 1090 liquid chromatograph equipped with a Hewlett-Packard 1073 A refractive index detector and styragel columns (HP PL gel 5 μm; pore size of 10^5, 10^4, 10^3, and 10^2 Å). Polystyrene (PS) standards and the M_n-(PCL) = 0.259 × M_n(PS)$^{1.073}$ equation[31] were used for calibration. ^{1}H NMR spectra were recorded in CDCl$_3$ with a Brucker AN 400 apparatus at 25°C. IR analysis was performed with a Perkin-Elmer 106 FTIR spectrometer. Differential scanning calorimetry (DSC) was carried out with a TA 2010 DSC thermal analyzer calibrated with indium. The melting temperature (T_m) was measured after cooling the sample down to −90°C and heating it up to 120°C at a 10°C min^{-1} rate. Transmission electron micrographs (TEM) were recorded with a Philips CM100 microscope equipped with a Gatan 673 CCD camera, and transferred to a computer equipped with the Kontron KS100 system. Samples were prepared by dipping a formvar-coated copper grid into a dilute micellar solution of the amphiphilic copolymer (0.5 wt%). The excess of solution was removed with a filter paper, followed by washing with water and drying in air.

Synthesis of four-arm star-shaped diblock copolyester 4a (Scheme 4): In a typical experiment, εCL (1.0 mL, 9 mmol), dry toluene (7 mL) and the spirocyclic tin initiator **1** (1.0 mL) in solution in toluene (0.025 M) were sequentially added into a previously flamed glass reactor through a rubber septum with a syringe. After 2 h at 40°C, the reaction mixture (1 mL) was picked out and hydrolyzed into star-shaped PCL **3** for characterization. The remaining polymerization mixture was added with a mixed solution of εCL (0.65 mL, 6.0 mmol) and αClεCL (0.56 g, 3.8 mmol) in dry toluene (4 mL). After stirring at 40°C for 2 h, the polymerization mixture was hydrolyzed by acetic acid (1 M in toluene), precipitated in cold heptane, collected by filtration and dried in vacuo.

Synthesis of 4b (Scheme 4): Compound **4a** (0.4 g, 0.5 mmol αClεCL units) was dissolved in DMF (12 mL), followed by addition of sodium azide (0.09 g, 1.4 mmol). After stirring at room temperature for 12 h, DMF was evaporated under reduced pressure, followed by addition of toluene (8 mL) and filtration of the solution that was poured in cold heptane. Polymer **4b** was recovered by filtration and dried in vacuo.

Synthesis of 4c (Scheme 4): Alkynyl end-capped PEO (CH$_3$O-(CH$_2$CH$_2$O)$_{24}$COCH$_2$CH$_2$C≡CH) (0.5 g, 0.46 mmol) and **4b** (0.33 g, 0.46 mmol αN$_3$εCL) were dissolved in THF (12 mL), followed by addition of triethylamine (0.1 mL, 0.68 mmol) and copper(I) iodide (0.03 g, 0.15 mmol). The reaction mixture was stirred at 35°C for 4 h. After cooling to room temperature, the solution was dropwise added to cold diethyl ether and collected by filtration. The polymer was dissolved in THF and purified by elution through SiO$_2$ (THF) in order to get rid of copper. Part of the solvent was evaporated, before the polymer was precipitated in diethyl ether, collected by filtration and dried in vacuo. Polymer **4c** was further purified by repeated precipitation in diethyl ether.

Synthesis of eight-shaped PCL 8 (Scheme 5): In a typical experiment, εCL (2.0 mL, 18 mmol), dry toluene (15 mL) and the spirocyclic tin initiator **1** (2.0 mL) solution in toluene (0.025 M) were sequentially added into a previously flamed glass reactor through a syringe. After 2 h at 40°C, αAεCL (0.42 g, 2.0 mmol) in toluene (2 mL) was added to the reactor, and the reaction temperature was increased up to 60°C. After 2 h, 3 mL of the reaction mixture was picked out and hydrolyzed into the parent star-shaped copolyester for characterization. The solution of the living spirocyclic precursor **6** was cooled down to room temperature under nitrogen, added with a benzophenone solution (2.6 mg, 17 μmol, in 0.6 mL toluene), and finally diluted with dry toluene until a copolyester concentration of 0.48 wt%. This solution was UV-irradiated (350–420 nm, 1000 W) at room temperature for 120 min. Part of the solvent was evaporated and half the solution was hydrolyzed by a few drops of acetic acid (1 M in toluene). The polymer **8** was precipitated in cold heptane, recovered by filtration and dried in vacuo for characterization. The second part of the solution, that is, the macroinitiator **7** (0.0214 mmol) was further used to resume the ring-expansion polymerization of a mixture of εCL and αClεCL.

Synthesis of 5a (Scheme 6): In a typical experiment, the macroinitiator **7** (0.021 mmol, concentration: 5 wt%) was added with a mixture of αClεCL (0.57 g, 3.9 mmol) and εCL (0.6 mL, 5.3 mmol) in dry toluene (4 mL). After stirring at 40°C for 2 h, the polymerization mixture (concentration: 9 wt%) was hydrolyzed by acetic acid (1 M in toluene), precipitated in cold heptane, collected by filtration and dried in vacuo.

Synthesis of 5b (Scheme 6): **5a** (0.4 g, 0.81 mmol αClεCL) was dissolved in DMF (10 mL), followed by addition of sodium azide (0.16 g, 2.43 mmol). After stirring at room temperature for 12 h, DMF was evaporated under reduced pressure, followed by addition of toluene (7 mL), filtration of the solution that was poured in cold heptane. The precipitated polymer **5b** was recovered by filtration and dried in vacuo.

Synthesis of 5c (Scheme 6): Alkynyl end-capped PEO (CH$_3$O-(CH$_2$CH$_2$O)$_{24}$COCH$_2$CH$_2$C≡CH) (0.69 g, 0.61 mmol) and **5b** (0.3 g, 0.61 mmol αN$_3$εCL) were dissolved in THF (12 mL), followed by addition of triethylamine (0.1 mL, 0.68 mmol) and copper(I) iodide (0.06 g, 0.30 mmol). The reaction mixture was stirred at 35°C for 4 h. After cooling to room temperature, the solution was dropwise added to cold diethyl ether and collected by filtration. The polymer was dissolved in toluene and purified by elution through SiO$_2$ (toluene) in order to get rid of copper. Part of the solvent was evaporated, before the polymer **5c** was precipitated in diethyl ether, collected by filtration and dried in vacuo. Precipitation of **5c** was repeated for sake of purification.

Micellization of 4c and 5c: Compound **4c** (or **5c**) (25 mg) was dissolved in THF (1.5 mL), followed by the dropwise addition of water (1 mL) under vigorous stirring for 2 h. Then water (2 mL) was added in order to freeze-in the micelles. The organic solvent (THF) was eliminated by dialysis against water. The micelles were observed by TEM.

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