Ring-Opening Polymerization of the Cyclic Ester Amide Derived from Adipic Anhydride and 1-Amino-6-hexanol in Melt and in Solution

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Summary: The ring-opening polymerization (ROP) of the cyclic ester amide (cEA) **5** (systematic name, 1-oxa-8-aza-cyclotetradecane-9,14-dione) – prepared from adipic anhydride and 1-amino-6-hexanol – in the melt at 165 °C and in solution at 100 °C and 120 °C with $Bu_2Sn(OMe)_2$ or $Ti(OBu)_4$ as initiator yields the alternating poly(ester amide) (PEA) **4** (systematic name, poly(5-(6-oxyhexylcarbamoyl)-pentanoate) with regular microstructure. Kinetic studies for different monomer-to-initiator ratios, different reaction media, initiators and temperatures reveal that the ROP is a first-order reaction with respect to the monomer. Under suitable polymerization conditions termination and transfer reactions are suppressed. The elementary chain growth reaction proceeds by a coordination insertion mechanism in analogy to the polymerization of lactones. By using monohydroxy- and bishydroxy-functional telechelic poly(ethylene oxide) and $Sn(octoate)_2$ as the initiating system poly(ethylene oxide)-*block*-poly(ester amide)s and poly(ester amide)-*block*-poly(ethylene oxide)-*block*-poly(ester amide)s are obtained. The poly(ester amide) **4** is a semicrystalline material with a melting point of 140 °C, the block copolymers are phase separated systems showing two melting points characteristic for the respective homopolymers.

Keywords: cyclic ester amides; kinetics; poly(ester amide)s; ring-opening polymerization

Introduction

Ring-opening polymerization (ROP) of depsipeptides[1] – six-membered cyclic ester amides from α-hydroxy acids and α-amino acids – has been studied intensively in the last decade.[2-12] ROP is usually performed in the melt at temperatures above 100 °C using transition metal initiators and proceeds according to a chain growth mechanism. The ROP of depsipeptides occurs via a coordination insertion mechanism which was studied in detail for the ROP of lactones.[13] The active species is generated upon acyl-oxygen cleavage under exclusive participation of the ester

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group. By using macro-initiators derived from poly(ethylene oxide) A-B and B-A-B block copolymers are obtained.[14-16]

Reports on ROP of cyclic ester amides with rings larger than six-membered have scarcely been mentioned in the literature. We prepared and polymerized different substituted eleven-membered cyclic ester amides of ε-amino caproic acids and β-hydroxy acids and a thirteen-membered cyclic ester amide of adipic acid and 1-amino-5-pentanol.[17,18]

In this paper results on ROP of a fourteen-membered cyclic ester amide - 1-oxa-8-aza-cyclotetradecane-9,14-dione (cEA **5**) - are reported with special emphasis on kinetic aspects. The possibility to prepare block copolymers by using macroinitiators for the ROP is presented.

Experimental Part

Materials. Adipic acid (Bayer AG) and 1-amino-6-hexanol (Fluka), were used as received. 5-(6-Hydroxy-hexylcarbamoyl)-pentanoic acid (**3**), 1-oxa-7-aza-cyclotridecane-8,13-dione (cEA **6**) and poly(ester amide) **4** were prepared according to the literature.[18,19] Before polymerization the monomer 1-oxa-8-aza-cyclotetradecan-9,14-dione (cEA, **5**) was sublimed at 120 °C and 10^{-2} mbar. The initiators titanium(IV) butoxide ($Ti(OBu)_4$, Acros), dibutyldimethoxytin(IV) ($Bu_2Sn(OMe)_2$, Aldrich), and tin(II) 2-ethylhexanoate ($Sn(octoate)_2$, Aldrich), were used without further purification. The monomer, initiators and purified reagents were stored under nitrogen. *N,N*-Dimethylformamide (DMF) and *N*-methyl-2-pyrrolidone (NMP) were refluxed over CaH_2 for several hours and distilled before use. The monohydroxy-functional poly(ethylene oxide)s (MPEO 2000, MPEO 5000, and MPEO 10000) and bishydroxy-functional poly(ethylene oxide)s (PEO 2000, PEO 6800 and PEO 11800) of narrow molecular weight distribution ($M_w/M_n \approx 1.1$) from Shearwater Polymers Inc. were used as received.

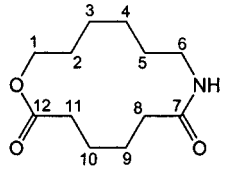
Polymerizations were carried out in an inert gas atmosphere. Nitrogen (Linde) was passed over molecular sieves (4 Å) and finely distributed potassium on aluminium oxide.

Measurements. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-300 FT-NMR spectrometer at 300 MHz and 75 MHz, respectively. Chloroform ($CDCl_3$), dimethylsulfoxide (DMSO-d_6) and trifluoroacetic acid (TFA-*d*) were used as solvents, and tetramethylsilane (TMS) served as an internal standard.

Gel permeation chromatography (GPC) analyses were carried out using a high pressure liquid chromatography pump (Bischoff HPLC pump 2200) and a refractive index detector (Waters 410). The eluting solvent was *N,N*-dimethylacetamide (DMAc) with 2.44 $g \cdot L^{-1}$ LiCl with a flow rate of 0.8 $mL \cdot min^{-1}$ at 80 °C. Four columns with MZ-DVB gel were applied: length of each column 300 mm, diameter 8 mm, diameter of gel particles 5 μm, and nominal pore widths 100 Å, 100 Å, 10^3 Å and 10^4 Å. Calibration was achieved using polystyrene standards of narrow molecular weight distribution from Polymer Standard Service Mainz.

Differential scanning calorimetric analyses were performed with a Netzsch DSC 204 under nitrogen with a heating rate of 10 $K \cdot min^{-1}$. Calibration was achieved using indium standard samples. Thermogravimetric analyses were performed on a TG 209 with a TA-System-Controller TASC 412/2 and kinetic software from Netzsch. IR spectra were recorded on a Perkin-Elmer FTIR 1760. C, H, N elemental analyses were performed with a Carlo Erba MOD 1106 instrument.

Preparation of 1-oxa-8-aza-cyclotetradecane-9,14-dione (cEA, 5). *Procedure A:* 5-(6-Hydroxy-hexylcarbamoyl)-pentanoic acid[19] (**3,** 6.36 g, 26.0 mmol) and $Ti(OBu)_4$ (170 mg, 0.5 mmol) were heated in vacuum for 16 d to 170 °C. The cyclic ester amide **5** was collected by sublimation. Yield: 86 % (5.06 g, 22.3 mmol). *Procedure B:* Poly(ester amide) **4** (1.13 g, 5.0 mmol) and $Ti(OBu)_4$ (34 mg, 0.1 mmol) were heated in vacuum for 16 d to 170 °C. The cyclic ester amide **5** was collected by sublimation. Yield: 75 % (856 mg, 3.8 mmol). Mp: 159-161 °C.



5

^{1}H NMR (DMSO-d_6): δ = 1.33 (m, 4H, CH_2-3/4); 1.41 (m, 2H, CH_2-5); 1.51 (m, 2H, CH_2-9); 1.59 (m, 4H, CH_2-2/10); 2.05 (tr, 2H, CH_2-8, ^3J = 6.0 Hz); 2.28 (tr, 2H, CH_2-11, ^3J = 6.4 Hz); 3.10 (d/tr, 2H, CH_2-6, ^3J = 5.3 Hz, ^3J = 5.7 Hz); 4.00 (tr, 2H, CH_2-1, ^3J = 5.3 Hz); 7.71 (br. s, 1H, NH) ppm.

^{13}C NMR (DMSO-d_6): δ = 23.90 (C-10, 1C); 24.80 (C-3/4, 1C); 25.49 (C-9, 1C); 25.53 (C-3/4, 1C); 26.56 (C-2, 1C); 27.89 (C-5, 1C); 34.13 (C-11, 1C); 35.46 (C-8, 1C); 36.94 (C-6, 1C); 63.84 (C-1, 1C); 171.69 (C-7/12, 1C); 172.57 (C-7/12, 1C) ppm.

^{1}H NMR ($CDCl_3$): δ = 1.44 (m, 4H, CH_2-3/4); 1.57 (m, 2H, CH_2-5); 1.67 (m, 4H, CH_2-2/9); 1.77 (m, 2H, CH_2-10); 2.26 (tr, 2H, CH_2-8, ^3J = 6.0 Hz); 2.37 (tr, 2H, CH_2-11, ^3J = 6.4 Hz); 3.36 (d/tr, 2H, CH_2-6, ^3J = 5.3 Hz, ^3J = 6.0 Hz); 4.12 (tr, 2H, CH_2-1, ^3J = 5.3 Hz); 5.64 (br. s, 1H, NH) ppm.

^{13}C NMR ($CDCl_3$): δ = 24.37 (C-10, 1C); 25.15 (C-3/4, 1C); 25.83 (C-3/4, 1C); 26.14 (C-9, 1C); 27.13 (C-2, 1C); 28.27 (C-5, 1C); 34.86 (C-11, 1C); 36.72 (C-8, 1C); 38.11 (C-6, 1C); 64.40 (C-1, 1C); 172.77 (C-7/12, 1C); 173.44 (C-7/12, 1C) ppm.

^{1}H NMR (TFA-*d*): δ = 1.60 (m, 4H, CH_2-3/4); 1.92 (m, 8H, CH_2-2/5/9/10); 2.62 (m, 2H, CH_2-8); 2.88 (m, 2H, CH_2-11); 3.75 (tr, 2H, CH_2-6, ^3J = 5.3 Hz); 4.35 (tr, 2H, CH_2-1, ^3J = 5.3 Hz) ppm.

^{13}C NMR (TFA-*d*): δ = 25.53 (C-10, 1C); 27.29 (C-3/4, 1C); 27.91 (C-3/4, 1C); 27.96 (C-9, 1C); 28.23 (C-2, 1C); 28.74 (C-5, 1C); 35.23 (C-11, 1C); 36.08 (C-8, 1C); 44.39 (C-6, 1C); 69.71 (C-1, 1C); 180.04 (C-7/12, 1C); 181.79 (C-7/12, 1C) ppm.

IR (KBr): 3303 (s); 2926 (s); 2862 (m); 1723 (s, C=O stretching, ester); 1643 (s, C=O stretching, amide I); 1547 (s, amide II); 1458 (m, O-CH_2); 1330 (m); 1288 (s); 1262 (m); 1232 (m); 1149 (s, C-O stretching); 1065 (m); 998 (w); 709 (m) cm^{-1}.

Anal. calcd for $C_{12}H_{21}NO_3$ (227.29): C, 63.41; H, 9.31; N, 6.16. Found: C, 63.35; H, 9.32; N, 6.05.

Ring-opening polymerization of cyclic ester amide 5. All glass vessels were heated in vacuo prior to use, filled with inert gas, and handled in a stream of dry inert gas. *Procedure A:* A mixture of cEA **5** (455 mg, 2.00 mmol) and $Bu_2Sn(OMe)_2$ (11.8 mg, 0.04 mmol) was heated to 165 °C. After 15 min the polymerization was terminated by cooling to room temperature (r.t.). The product was dissolved at 60 °C in DMF (8 mL) and precipitated in 150 mL diethyl ether. The polymer was isolated by filtration as a colourless solid. Yield: 93 % (423 mg). GPC: M_n = 18100, M_w = 29700, M_w/M_n = 1.64. *Procedure B*: A solution of cEA **5** (341 mg, 1.50 mmol) in DMF (410 μL) was heated to 100 °C and treated with $Bu_2Sn(OMe)_2$ (4.4 mg, 0.015 mmol) for initiation. After 96 h the polymerization was terminated by cooling to r.t. The reaction mixture was diluted with additional DMF (0.6 mL) and precipitated in ether (30 mL). The polymer **4** was isolated by filtration as a colourless solid. Yield: 98 % (335 mg). GPC: M_n = 18400, M_w = 37500, M_w/M_n = 2.04

^{1}H NMR (DMSO-d_6): δ = 1.26 (m, 4H, CH_2-3/4); 1.36 (m, 2H, CH_2-5); 1.48 (m, 4H, CH_2-9/10); 1.54 (m, 2H, CH_2-2); 2.04 (m, 2H, CH_2-8); 2.27 (m, 2H, CH_2-11); 3.00 (d/tr, 2H, CH_2-6, ^3J = 6.0 Hz); 3.98 (tr, 2H, CH_2-1, ^3J = 6.4 Hz); 7.75 (br. s, 1H, NH) ppm.

^{13}C NMR (DMSO-d_6): δ = 24.03 (C-9, 1C); 24.69 (C-3/4, 1C); 25.03 (C-10, 1C); 25.96 (C-3/4, 1C); 28.02 (C-2/5, 1C); 28.95 (C-2/5, 1C); 33.17 (C-11, 1C); 34.93 (C-8, 1C); 38.19 (C-6, 1C); 63.55 (C-1, 1C); 171.53 (C-7/12, 1C); 172.73 (C-7/12, 1C) ppm.

^{1}H NMR (DMSO-d_6, 100 °C): δ = 1.32 (m, 4H, CH_2-3/4); 1.43 (m, 2H, CH_2-5); 1.55 (m, 6H, CH_2-2/9/10); 2.06 (m, 2H, CH_2-8); 2.28 (m, 2H, CH_2-11); 3.05 (d/tr, 2H, CH_2-6, ^3J = 6.0 Hz); 4.02 (tr, 2H, CH_2-1, ^3J = 6.4 Hz); 7.39 (br. s, 1H, NH) ppm.

^{13}C-NMR (DMSO-d_6, 100 °C): δ = 23.52 (C-9, 1C); 24.06 (C-3/4, 1C); 24.39 (C-10, 1C); 25.31 (C-3/4, 1C); 27.49 (C-2/5, 1C); 28.33 (C-2/5, 1C); 32.79 (C-11, 1C); 34.47 (C-8, 1C); 37.84 (C-6, 1C); 62.92 (C-1, 1C); 170.97 (C-7/12, 1C); 171.85 (C-7/12, 1C) ppm.

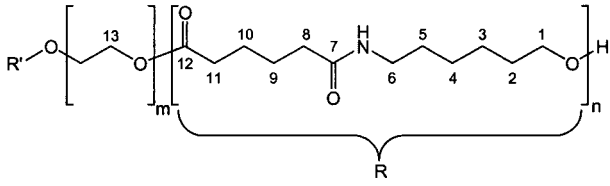
^{1}H NMR (TFA-*d*): δ = 1.51 (m, 4H, CH_2-3/4); 1.79 (m, 4H, CH_2-2/5); 1.87 (m, 4H, CH_2-9/10); 2.60 (m, 2H, CH_2-8); 2.83 (m, 2H, CH_2-11); 3.63 (tr, 2H, CH_2-6, ^3J = 7.2 Hz); 4.28 (tr, 2H, CH_2-1, ^3J = 6.8 Hz) ppm.

^{13}C NMR (TFA-*d*): δ = 25.22 (C-9, 1C); 26.98 (C-3/4/10, 2C); 27.96 (C-3/4, 1C); 29.52 (C-2/5, 1C); 29.79 (C-2/5, 1C); 35.04 (C-11, 1C); 35.16 (C-8, 1C); 44.98 (C-6, 1C); 68.74 (C-1, 1C); 180.42 (C-7/12, 1C); 180.98 (C-7/12, 1C) ppm.

IR (KBr): 3314 (s); 3086 (w); 2937 (s); 2863 (s); 1735 (s, C=O stretching, ester); 1640 (s, C=O stretching, amide I); 1546 (s, amide II); 1465 (m, O-CH_2); 1420 (m); 1373 (m); 1269 (s); 1176 (s, C-O stretching); 1073 (w); 969 (w); 731 (m); 581 (w) cm^{-1}.

For kinetic measurements after selected reaction times samples were drawn in a stream of dry inert gas and analyzed by means of NMR and GPC.

Ring-opening polymerization of cyclic ester amide 5 using poly(ethylene oxide) MPEO 2000 and Sn(octoate)$_2$ as initiator. Poly(ethylene oxide) MPEO 2000 (80 mg, 0.04 mmol) and Sn(octoate)$_2$ (186 μL of a 0.215 M solution in toluene, 0.04 mmol) were stirred for 45 min at 145 °C. Cyclic ester amide **5** (681 mg, 3.00 mmol) and 500 μL of toluene were added at r.t. to this mixture. To obtain a homogeneous system the mixture was heated to 145 °C, cooled again to r.t. and toluene was removed at reduced pressure. For polymerization the mixture was stirred for 48 h at 165 °C. The polymerization was terminated by cooling to r.t. The product was dissolved in DMAc (5 mL) at 60 °C, precipitated in diethyl ether (150 mL) and isolated by filtration. To remove unconverted macroinitiator the solid product was washed with water; from the resulting suspension the polymer was isolated by centrifugation. Yield: 715 mg (94 %). GPC: M_n = 20600, M_w = 38100, M_w/M_n = 1.85.



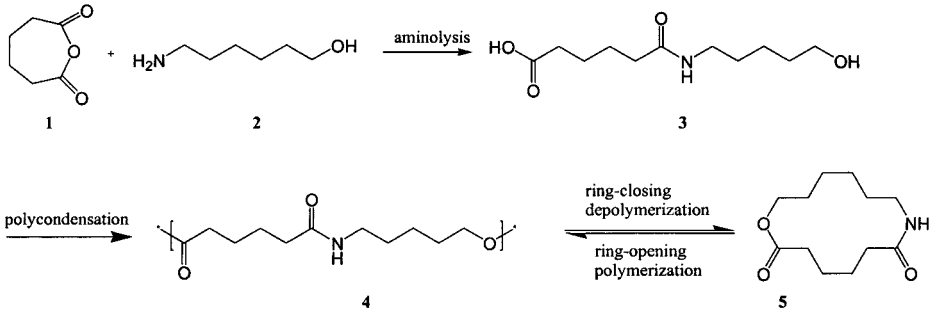
R' = Me for A-B block copolymer; R' = R for B-A-B block copolymer

^{1}H NMR (DMSO-d_6, 100 °C): δ = 1.34 (m, 4H, CH_2-3/4); 1.44 (m, 2H, CH_2-5); 1.56 (m, 6H, CH_2-2/9/10); 2.09 (m, 2H, CH_2-8); 2.28 (m, 2H, CH_2-11); 3.06 (d/tr, 2H, CH_2-6, ^3J = 6.0 Hz, ^3J = 6.8 Hz); 3.56 (s, 4H, CH_2-13); 4.03 (tr, 2H, CH_2-1, ^3J = 6.8 Hz); 7.32 (br. s, 1H, NH) ppm.

^{13}C NMR (DMSO-d_6, 100 °C): δ = 24.03 (C-9, 1C); 24.67 (C-3/4, 1C); 25.03 (C-10, 1C); 25.94 (C-3/4, 1C); 28.02 (C-2/5, 1C); 29.94 (C-2/5, 1C); 33.17 (C-11, 1C); 34.93 (C-8, 1C); 38.19 (C-6, 1C); 63.57 (C-1, 1C); 69.71 (C-13, 1C); 171.53 (C-7/12, 1C); 172.71 (C-7/12, 1C) ppm.

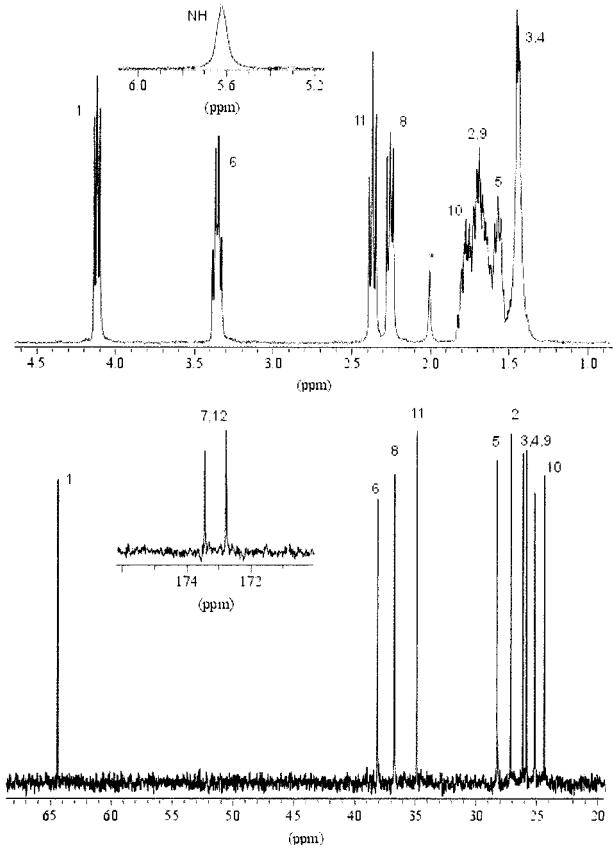
Results and Discussion

Monomer Synthesis. In a previous paper we have studied the catalytic polycondensation of 5-(6-hydroxy-hexylcarbamoyl)-pentanoic acid (**3**) in the temperature range of 110 °C to 170 °C.[19] Up to 140 °C the polycondensation results in high yields of poly(ester amide) **4**, however, at 170 °C the polymer yield reaches a maximum after 90 min, then due to back-biting reactions the yield decreases in favour of the cyclic ester amide **5**. We have successfully applied ring-closing depolymerization for the synthesis of cEA **5**, a monomer suitable for ring-opening polymerzation. As starting material for the synthesis served adipic anhydride (**1**) and 1,6-amino hexanol (**2**) which in a selective reaction in solution result in 5-(6-hydroxy-hexylcarbamoyl)-pentanoic acid (**3**) (Scheme 1). Preparation of the cyclic ester amide was performed either in a one pot synthesis starting with the α-carboxy-ω-hydroxy amide **3** (procedure A) or starting with the poly(ester amide) **4** (procedure B); $Bu_2Sn(OMe)_2$ or $Ti(OBu)_4$ served as catalyst. The yields of cEA **5** were similar for both procedures and reached values from 75 to 86 %. The cyclic ester amide is a colourless solid with a melting point of 159 - 161 °C.



Scheme 1. Synthesis and ring-opening polymerization of cyclic ester amide (cEA) **5**.

The ^{1}H and ^{13}C NMR spectra (Figure 1), the IR spectrum and the elemental analysis clearly reveal the cyclic nature of the product. Of special interest in the NMR spectra are the methylene groups adjacent to the functional groups with characteristic resonance lines: CH_2O (δ = 4.12 ppm, 64.40 ppm), CH_2NH (δ = 3.36 ppm, 38.11 ppm), CH_2COO (2.37 ppm, 34.86 ppm) and CH_2CONH (δ = 2.26 ppm, 36.72 ppm). Since all these groups show only one resonance signal a uniform microstructure is expected. The NMR spectra of cEA **5** in DMSO-d_6 and TFA-*d* are given in the experimental part, to be compared with that of the poly(ester amide) **4** which is insoluble in $CDCl_3$.



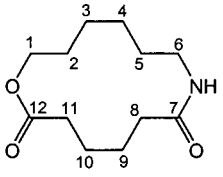


Figure 1. ^{1}H and ^{13}C NMR spectrum of cEA **5** in $CDCl_3$.

Ring-opening polymerization. The ROP of cEA **5** was performed in the melt above the melting temperature of the monomer at 165 °C and in solution of DMF or NMP with $Bu_2Sn(OMe)_2$ or $Ti(OBu)_4$ as the initiator (Table 1).

Table 1. Reaction conditions and results of the ROP of cEA **5** in the melt and in solution

No.	Initiator	$[M]_0/[I]_0$	Solvent	T/°C	t/min	M_n [a]	M_w/M_n [a]	X_p/% [b]
1	$Bu_2Sn(OMe)_2$	50	-	165	15	21300	1.79	99
2	$Bu_2Sn(OMe)_2$	100	-	165	60	32800	1.89	96
3	$Bu_2Sn(OMe)_2$	250	-	165	360	22000	1.91	76
4	$Bu_2Sn(OMe)_2$	50	-	145	60	23900	1.81	98
5	$Bu_2Sn(OMe)_2$	50	DMF	100	24	8700	1.62	70
6	$Bu_2Sn(OMe)_2$	50	DMF	120	2	15700	2.10	91
7	$Bu_2Sn(OMe)_2$	50	NMP	100	24	7900	1.60	77
8	$Ti(OBu)_4$	50	DMF	100	0.5	11000	1.69	95

[a] determined by means of GPC in DMAc; [b] determined by ^{1}H NMR-spectroscopy in TFA-*d*; [c] $[M]_0$ = 3.66 mol/L.

In the melt with $Bu_2Sn(OMe)_2$ as the initiator the polymer yields obtained at $[M]_0/[I]_0$ = 50 and 100 are > 95 %, at lower initiator concentration ($[M]_0/[I]_0$ = 250) the yields achieve a value of 76% after 6 h. With increasing the $[M]_0/[I]_0$ ratio the molecular weight increases indicating a controlled polymerization, however, the polydispersities of the polymers are relatively high. This is explained by transesterification reactions which eventually lead to a most probable chain length distribution without changing the microstructure of the alternating poly(ester amide). In solution with $Bu_2Sn(OMe)_2$ as the initiator at short reaction times the polymer yields are higher than at longer reaction times. This is interpreted in the sense that in the kinetically controlled regime of the reaction high molecular weight polymer is produced and in the thermodynamic controlled regime due to the monomer - polymer equilibrium cyclic oligomers are produced.

The influence of $[M]_0/[I]_0$ ratio, temperature, and initiator on the course of the reaction was studied by selective kinetic measurements. All poly(ester amide)s (PEA) prepared show a unimodal molecular weight distribution in GPC analyses (Figure 2). The GPC of the PEA prepared in solution clearly shows a single well resolved oligomeric series. The ^{1}H NMR spectrum shows characteristic resonance lines for an alternating poly(ester amide); the chemical shifts of the characteristic groups adjacent to the functional groups are clearly shifted to higher fields as

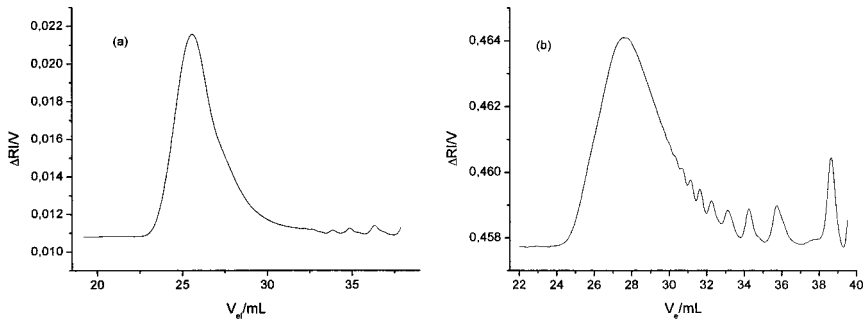


Figure 2. GPC of poly(ester amide)s **4** in DMAc / 2.44 g·L^{-1} LiCl: (a) Prepared in melt at T = 165 °C with $Bu_2Sn(OMe)_2$ as the initiator, $[M]_0/[I]_0$ = 100 (M_n = 32800, table 1, no. 2). (b) Prepared in DMF solution at T = 100 °C with $Ti(OBu)_4$ as the initiator $[M]_0/[I]_0$ = 50 (M_n = 11000, table 1, no. 8).

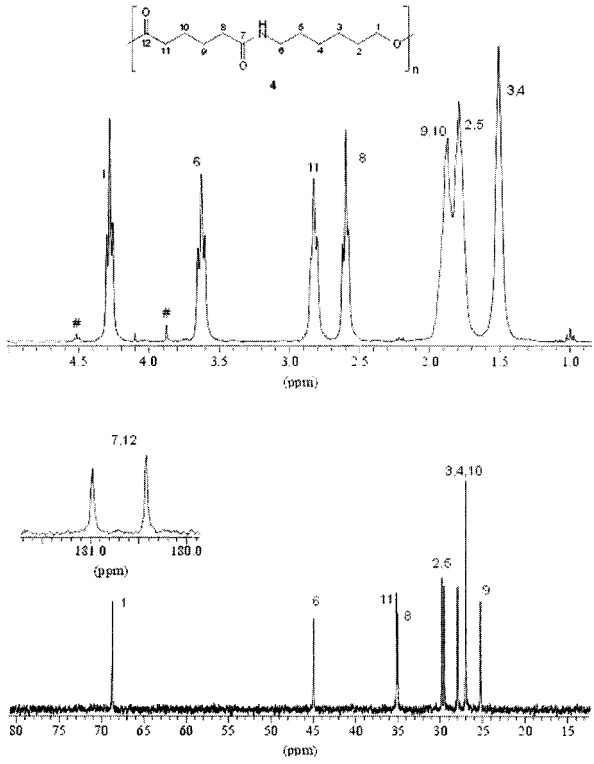


Figure 3. ^{1}H and ^{13}C NMR spectrum of poly(ester amide) **4** in TFA-*d* (# = end group).

compared to the chemical shifts of the cyclic monomer (Figure 3).

The existence of only one signal in the ^{13}C NMR spectrum for each carbon is indicative for the regular alternating microstructure of the poly(ester amide) **4**. The signals of small intensity in the ^{1}H NMR spectrum at δ = 3.88 ppm and δ = 4.55 ppm were assigned to -COO*CH*$_3$ and -*CH*$_2$OCOCF$_3$ end groups.

The poly(ester amide) **4** is a semicrystalline material with a melting point of 140 °C. The endotherm at the melting transition may show two peaks or one peak with a shoulder, indicating the existence of two crystalline modifications. The thermal stability of poly(ester amide) **4** was determined by thermogravimetric analysis: a 5 % mass loss is observed at 278 °C, a 50 % mass loss is observed at 387 °C, and a 90 % mass loss at 432 °C.

Kinetic Aspects. For the kinetic analysis at selected reaction times samples were analyzed; by means of ^{1}H NMR spectroscopy the monomer conversion and by means of GPC the number average molecular weight were determined. The monomer conversion was obtained by comparison of the integrals of the CH_2O group of the monomer and the polymer. The influence of different parameters on the kinetics of the ROP of cEA **5** were investigated: The influence of the monomer-to-initiator ratio was studied for $[M]_0/[I]_0$ = 50, 100 and 250 at 165 °C in the melt with $Bu_2Sn(OMe)_2$ as the initiator. Polymerization in solution of DMF and NMP was compared with the polymerization in bulk. The influence of the temperature on the polymerization in DMF solution was studied with $Bu_2Sn(OMe)_2$ as the initiator. The polymerization rates of the ROP with $Bu_2Sn(OMe)_2$ and $Ti(OBu)_4$ as initiators in DMF solution at 100 °C were compared. Finally a comparison of the ROP of the fourteen-membered cEA **5** 1-oxa-8-aza-cyclotetradecane-9,14-dione - with the thirteen-membered cEA **6** - 1-oxa-7-aza-cyclotridecane-8,13-dione - in DMF solution was performed.

Ring-opening polymerization in bulk. Influence of the monomer/initiator ratio. For a controlled polymerization it is expected that with decreasing initiator concentration the degree of polymerization (P_n) increases according to: $P_n = [M]_0 \cdot X_p / [I]_0$, where $[M]_0$ is the initial monomer concentration, $[I]_0$ the initial initiator concentration and X_p the conversion. The first-order plots for the polymerization of cEA **5** in the melt with $Bu_2Sn(OMe)_2$ as the initiator are linear for ($[M]_0/[I]_0$ = 50 and 100 up to high conversion (Figure 4a). For $[M]_0/[I]_0$ = 250 the plot is linear up to 120 min, however the conversion increases slowly. From the slope of the straight lines the

apparent rate constants were determined to be $k[P^*] = 77.7 \cdot 10^{-4}$ s^{-1} for $[M]_0/[I]_0 = 50$, $24.1 \cdot 10^{-4}$ s^{-1} for $[M]_0/[I]_0 = 100$, and $0.7 \cdot 10^{-4}$ s^{-1} for $[M]_0/[I]_0 = 250$. These results indicate that with decreasing the initiator concentration the efficiency of the initiator decreases. In order to obtain information on transfer reactions the dependence of M_n on conversion was studied (Figure 4b). The values obtained by GPC using PS standards are not absolute values; however, a linear dependence of M_n on conversion is a proof of the absence of transfer reactions. For $[M]_0/[I]_0 = 50$ and 100 we observe a linear dependence up to quantitative conversion. For $[M]_0/[I]_0 = 250$ where the concentration of active species is lowest, deviations form linearity are observed starting with a conversion of 30 %. We have excluded the possibility of a thermal polymerization since at 165 °C the cyclic monomer is stable for at least 3 h. It should be mentioned that the M_n vs. conversion plots do not pass through the origin which is tentatively explained by the method of determination of M_n by GPC using polystyrene standards and the relative high molecular weight of the monomer/initiator adduct.

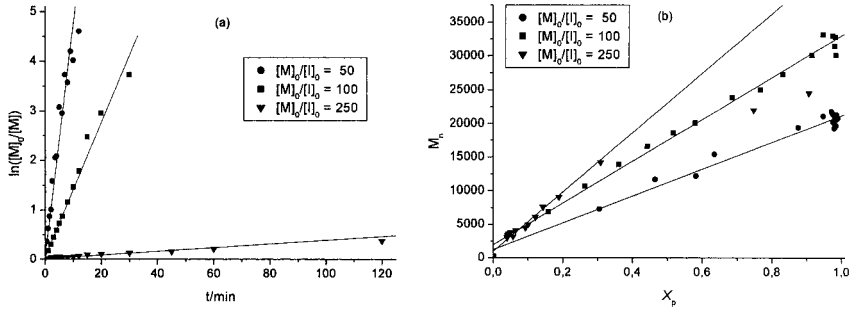


Figure 4. ROP of cEA **5** in bulk for different monomer-to-initiator ratios (T = 165 °C, initiator $Bu_2Sn(OMe)_2$): (a) First-order plot; (b) M_n vs. conversion.

Ring-opening polymerization in solution. (i) Influence of the solvent. The poly(ester amide) **4** is soluble only in aprotic dipolar solvents. We have performed the polymerization of cEA **5** in DMF and in NMP as a solvent with $Bu_2Sn(OMe)_2$ under identical conditions: T = 100 °C, $[M]_0$ = 3.66 mol/L and $[M]_0/[I]_0 = 50$. First-order plots show that in DMF as the solvent the conversion increases faster than in NMP as the solvent up to a conversion of 50 % (Figure 5a). The molecular weight increases linear up to this conversion, too (Figure 5b). Both solvents are not

really inert solvents. At longer reaction times and decreasing monomer concentration transfer to solvent is to be expected.

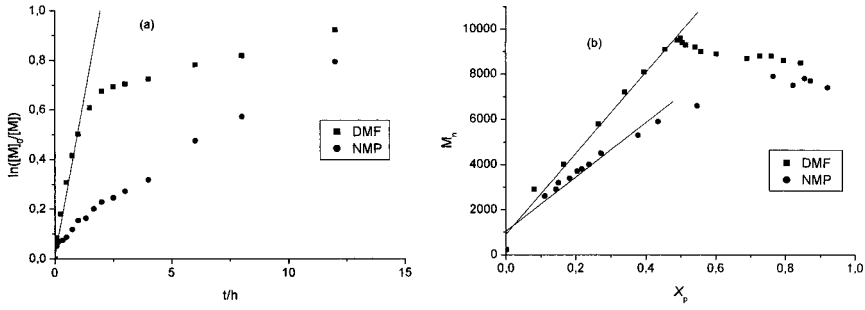


Figure 5. ROP of cEA **5** in solution for different solvents. (initiator: $Bu_2Sn(OMe)_2$, $[M]_0/[I]_0$ = 50, T = 100 °C, $[M]_0$ = 3.66 mol·L^{-1}). (a) First-order plot; (b) M_n vs. conversion.

(ii) Influence of the temperature. The influence of temperature on the ROP of the cEA **5** was studied for the polymerization in DMF solution and $Bu_2Sn(OMe)_2$ as initiator at a monomer-to-initiator ratio of $[M]_0/[I]_0$ = 50 for temperatures of 100 °C and 120 °C. For both temperatures the conversion increases rapidly within the first two hours: for T = 120 °C after 2h a conversion of 95 % is reached, for T = 100 °C the conversion increases fast to ca. 50 % within the first two hours.

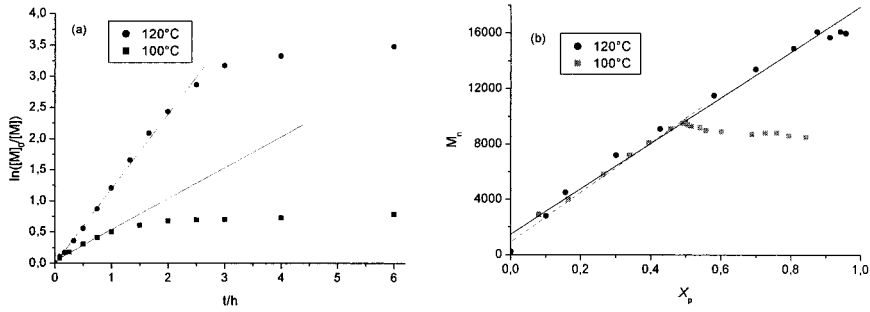


Figure 6. ROP of cEA **5** in DMF-solution at different temperatures. (initiator: $Bu_2Sn(OMe)_2$, $[M]_0/[I]_0$ = 50, $[M]_0$ = 3.66 mol·L^{-1}). (a) First-order plot; (b) M_n vs. conversion.

A first-order plot (Figure 6a) shows a linear dependence at T = 120 °C up to high conversion and at T = 100 °C only up to a conversion of 50 %. The conclusion from this result is that with increasing temperature the rate of polymerization increases faster than the rate of adventitious termination caused by the solvent. From the slope of the straight lines the apparent rate constants were determined to be $k[P^*] = 1.5 \cdot 10^{-4}$ s^{-1} (at 100 °C) and $3.2 \cdot 10^{-4}$ s^{-1} (at 120 °C). The dependence of the number average-molecular weight on conversion is linear up to 95 % conversion at 120 °C and up to 50 % conversion for 100 °C (Figure 6b). This means that at 100°C transfer reactions are observed starting with a conversion of 50 %. At 120 °C there is no indication of transfer reactions. In conclusion, the polymerization of cEA **5** in DMF solution with $Bu_2Sn(OMe)_2$ as the catalyst at 120 °C is a controlled polymerization since the first-order plot is linear and the molecular weight increases linearly up to high conversion. No transfer or termination reactions are observed. At higher temperatures the rate of polymerization is faster than that of transfer and termination reactions.

(iii) Influence of the initiator. The influence of the two initiators $Bu_2Sn(OMe)_2$ and $Ti(OBu)_4$ on the polymerization of cEA **5** was investigated at 100 °C in DMF solution. Within two hours with $Ti(OBu)_4$ as the catalyst complete conversion is obtained while with $Bu_2Sn(OMe)_2$ the conversion is only 50 %. A first-order kinetic plot (Figure 7a) for the linear part reveals an apparent rate constant of $k[P^*] = 22.2 \cdot 10^{-4}$ s^{-1} for $Ti(OBu)_4$ and $k[P^*] = 1.5 \cdot 10^{-4}$ s^{-1} for $Bu_2Sn(OMe)_2$ as initiator.

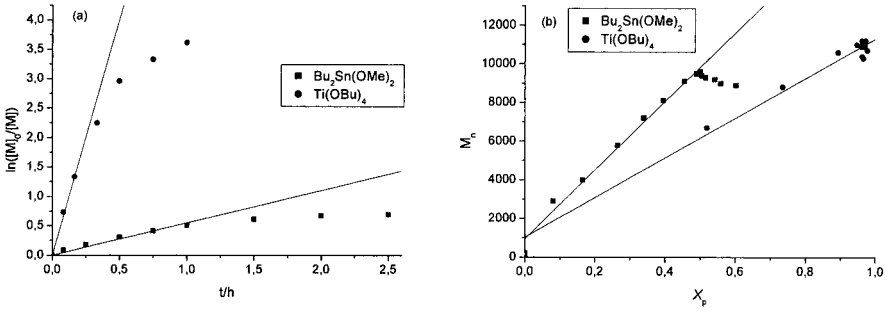


Figure 7. ROP of cEA **5** in DMF-solution with $Bu_2Sn(OMe)_2$ and $Ti(OBu)_4$ as the initiators. ($[M]_0/[I]_0 = 50$, T = 100 °C, $[M]_0 = 3.66$ mol·L^{-1}). (a) First- order plot; (b) M_n vs. conversion.

The dependence of the molecular weight on conversion is linear up to high conversions for $Ti(OBu)_4$ and up to 50 % conversion for $Bu_2Sn(OMe)_2$ as initiator (Figure 7b). At equal conversion the molecular weight obtained with $Ti(OBu)_4$ is lower by a factor of about two. This is expected since the number of chains initiated by $Ti(OBu)_4$ is two times higher.

Polymerization of cyclic ester amides with fourteen- and thirteen-membered rings. In a previous paper[18] we have studied the ring-opening polymerization of cEA **6** in the melt and found for $Bu_2Sn(OMe)_2$ as initiator ($[M]_0/[I]_0$ = 100) at 160 °C an apparent rate constant of $k[P^*]$ = 20.4 $\cdot 10^{-4}$ s^{-1} which is very close to the value obtained for the cEA **5** at 165 °C, $k[P^*]$ = 24.1$\cdot 10^{-4}$ s^{-1}. In solution we have studied the polymerization of the two monomers at 100 °C in DMF as solvent. Both the first-order plots (Figure 8a) and the M_n vs. conversion plots (Figure 8b) are identical within experimental error.

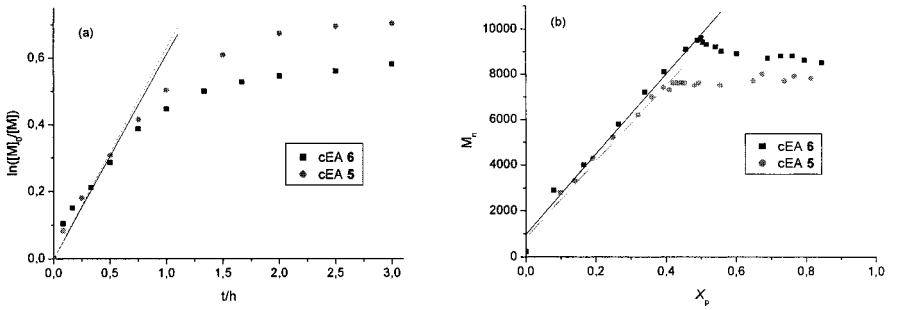
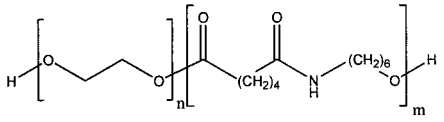


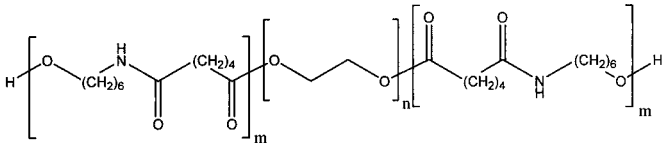
Figure 8. ROP of cEA **5** and **6** in DMF-solution. (initiator: $Bu_2Sn(OMe)_2$ $[M]_0/[I]_0$ = 50, T = 100 °C, $[M]_0$ = 3.66 mol·L^{-1}). (a) First-order plot; (b) M_n vs. conversion.

Synthesis and characterization of block copolymers. A-B and B-A-B block copolymers with A the poly(ethylene oxide) block and B the poly(ester amide) block have been prepared before by polymerization of cyclic ester amide **6** with an initiating system comprising hydroxytelechelic poly(ethylene oxide) and $Sn(octoate)_2$.[19] For the synthesis of A-B and B-A-B block copolymers comprising an alternating poly(ester amide) block with adipic acid and 1-amino-6-hexanol repeating units and a poly(ethylene oxide) block (cf. below) the cyclic ester amide **5** was polymerized with monohydroxy-functional poly(ethylene oxide)s (MPEO) and bishydroxy-functional poly(ethylene oxide)s (PEO) of various molecular weights in combination with $Sn(octoate)_2$ as catalyst ($[Sn(octoate)_2]/[OH]$ = 1). In order to activate all hydroxyl groups and to

initiate all chains at the same time poly(ethylene oxide) was first treated with $Sn(octoate)_2$ to generate the active species, then the monomer was added ($[cEA]_0/[OH]_0 = 75$) and the mixture was heated to 165 °C for polymerization. For termination and purification the mixture was cooled to room temperature dissolved in DMF and precipitated in diethyl ether (Table 2).



poly(ethylene oxide)-*block*-poly(ester amide)



poly(ester amide)-*block*-poly(ethylene oxide)-*block*-poly(ester amide)

Table 2. Reaction conditions and results for the ROP of cEA **5** with poly(ethylene oxide) macroinitiators and $Sn(octoate)_2$ as catalyst in melt at T = 165 °C, t = 48 h, $[cEA]/[OH] = 75$, $[Sn(octoate)_2]/[OH] = 1$

No.	PEO	X_p of cEA in %[a]	PEO in wt.%[b]	PEO in wt.%[c]	M_n[d] (M_w/M_n)	Yield in %[e]
1	MPEO 2000	99	11	8	20600 (1.85)	94
2	MPEO 5000	95	23	11	18300 (1.76)	76
3	MPEO 10000	93	37	38	24100 (1.72)	65
4	PEO 2000	98	6	5	22400 (1.83)	95
5	PEO 6800	95	17	10	18500 (1.94)	83
6	PEO 11800	93	26	13	20600 (1.96)	74

[a] determined by means of ^1H NMR spectroscopy of the crude product; [b] percent by weight of PEO in the feed; [c] percent by weight of PEO in the block copolymer determined by means of ^1H NMR spectroscopy after purification of the product; [d] determined by means of GPC in DMAc; [e] determined by weight.

The conversion of the cEA **5** is higher than 90 % in all cases; however, the efficiency of the initiating PEO block decreases with increasing molecular weight of the macroinitiator. This is

reflected by the decreasing block copolymer yield and the composition of the block copolymer. The composition of the purified copolymers was determined by ^{1}H NMR spectroscopy (Figure 9). Beside the resonances for the poly(ester amide) blocks assigned before, the singlet at δ = 3.56 ppm is assigned to the ethylene oxy repeating units of the poly(ethylene oxide) block.

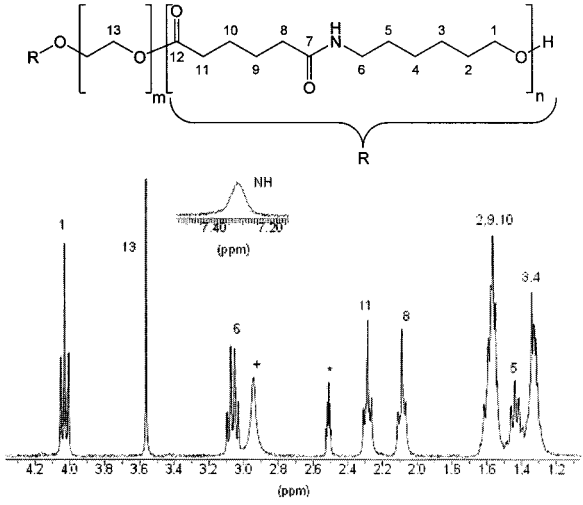


Figure 9. ^{1}H NMR spectrum of the B-A-B triblock copolymer (table 2, no. 4) (DMSO-d_6/100°C).

The GPC analysis of the block copolymers (Figure 10) shows a monomodal distribution of the molecular weight with no residual macroinitiator in the purified product.

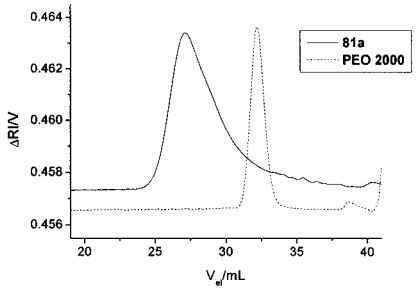


Figure 10. GPC elution curve of the B-A-B triblock copolymer (table 2, no. 4) and of the corresponding macroinitiator PEO 2000 in DMAc / 2.44 g·L^{-1} LiCl.

The thermal characteristics of these block copolymers as determined by DSC measurements reveal a phase separated system with two melting points. For the block copolymer - entry 5 of table 2 - the poly(ester amide) domains show a melting point of T_m = 136 °C with a melting enthalpy of ΔH_m = 42.5 J/g which is very close to the melting point of the homopolymer (T_m = 140 °C, ΔH_m = 53.6 J/g), and in addition show a melting point of 60 °C for the poly(ethylene oxide) domains.

Conclusions

Ring-opening polymerization of cEA **5** occurs with high rate up to high conversion above the melting point of the monomer. In solution of aprotic dipolar solvents transfer and termination reactions can not completely be excluded. However, DMF should be favoured over NMP, higher temperatures (120 °C) should be preferred over lower temperatures (100 °C) and $Ti(OBu)_4$ should be given preference compared to $Bu_2Sn(OMe)_2$ as initiator. Further, the kinetic data show that the polymerization in bulk and under certain conditions in solution is controlled. As a consequence block copolymers were prepared.

Acknowledgement

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