The synthesis and polymerization of oxo-crown ethers

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A novel synthetic route to and a polymerization procedure for oxo-crown ethers 2,11-dioxo-18-crown-6 (**1**), 2-oxo-12-crown-4 (**2**) and 2-oxo-21-crown-7 (**3**) are described. Cyclization of the ω-hydroxycarboxylic acid precursors of **1–3** has been achieved by heating these precursors in the presence of a Lewis acid catalyst ($CoCl_2$) and a template salt (MCl). Cyclization yields up to 82% were reached, using CsCl as template salt. Oxo-crown ethers **1–3** have been polymerized using $SnOct_2$ as catalyst, giving polymers with molecular weights of approximately 5 kg/mol and dispersities of ca. 1.8 (measured with polyethylene oxide standards). The polymerization of **2** was monitored with ^{1}H-NMR and SEC giving information about (a) the influence of monomer/catalyst ratio and temperature on polymerization rate and (b) the influence of temperature on molecular weight (distribution). The possibility of introducing endgroups into poly(2-oxo-12-crown-4) using $SnOct_2$-catalyzed polymerization was also studied.

1. Introduction

Almost thirty years after their discovery in 1967 by Pedersen [1], crown ethers are still among the most important building blocks in supramolecular chemistry. Since that time a wide range of crown ethers has been synthesized and reviews have been published giving an overview of the syntheses and properties of crown ethers [2]. Recently, crown ethers have been used as threading rings in polyrotaxanes, indicating the versatility of these compounds in macromolecular chemistry [3].

In the family of crown ethers, medium-sized oxo-crown ethers have received only limited attention. Thus far, only Okahara et al. [4] have reported several of these compounds, including 2,11-dioxo-18-crown-6 (**1**), 2-oxo-12-crown-4 (**2**) and 2-oxo-21-crown-7 (**3**), which are shown in Fig. 1. These compounds were synthesized in one-step procedures in yields of 18%, 36% and 23% for **1**, **2** and **3**, respectively. Surprisingly, medium-sized crown ethers have never been used in ring opening polymerization reactions, although polymerizations of related ether-lactones have been reported [5]. Stannyl compounds – typically stannous octanoate ($SnOct_2$) – have been applied as catalysts in these polymerizations, and a few ether-lactone monomers could be converted into biodegradable polymers using these catalysts.
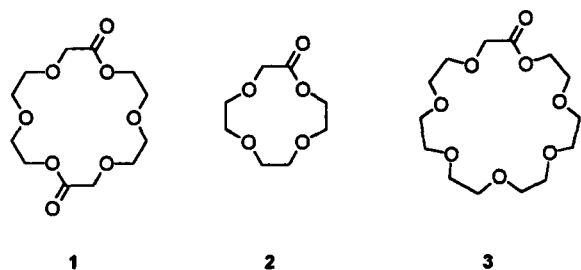

Fig. 1. 2,11-Dioxo-18-crown-6 (**1**); 2-oxo-12-crown-4 (**2**) and 2-oxo-21-crown-7 (**3**).

In this paper, a new synthetic route to the oxo-crown ethers **1–3** – including a convenient cyclization procedure of the ω-hydroxycarboxylic acid precursors – as well as their polymerization with $SnOct_2$ are presented.

2. Results and discussion

2.1. Synthesis of oxo-crown ethers 1–3

The synthetic route to the different ω-hydroxycarboxylic acid precursors **8 a–8 c** is shown in Fig. 2. Monobenzylation of di- and triethylene glycol **4 a** and **4 b** was achieved using a four-fold excess of glycol [6]. For the monobenzylation of hexaethylene glycol **4 c**, a method reported by Mahboobi [7] was preferred, since this procedure required only a two-fold excess of glycol. Monobenzylated products **5 a**, **5 b** and **5 c** could be isolated in yields of 65%, 67% and 70%, respectively.
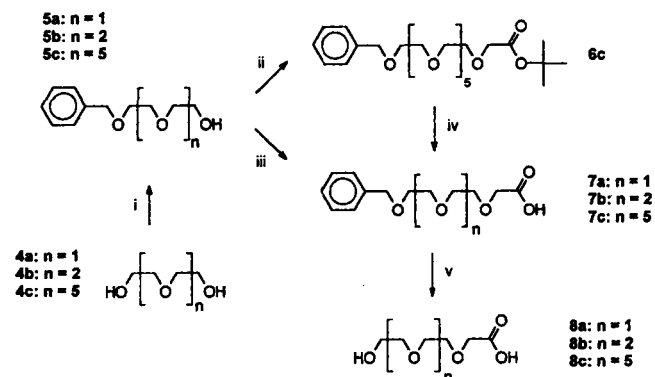
Fig. 2. The synthesis of the ω-hydroxycarboxylic acid precursors (**8 a–8 c**). i. BnCl, NaOH, water, Δ (n = 1,2) or BnCl, tBuOK, dioxane, Δ (n = 5); ii. $BrCH_2COOt$Bu, tBuOK, tBuOH; iii. $BrCH_2COOH$, tBuOK, DMF; iv. TFA; v. Pd/C, H_2, HCl, dioxane, water.

Monobenzyl di- and triethylene glycol were coupled with bromoacetic acid, yielding carboxylic acids **7 a** and **7 b** directly. The reactions were carried out in DMF using 2 equivalents of *tert*-BuOK as base. After aqueous work-up **7 a** and **7 b** were obtained in isolated yields of 55% and 76%, respectively. Monobenzyl hexaethylene glycol **5 c** was coupled with bromoacetic acid *tert*-butyl ester in *tert*-butanol using *tert*-BuOK as base. After column chromatography the *tert*-butyl ester **6 c** was obtained in a 70% yield. Conversion to carboxylic acid **7 c** was accomplished by hydrolysis in TFA. Aqueous work-up afforded **7 c** in a 86% yield. Catalytic hydrogenation of compounds **7 a–7 c** gave the ω-hydroxycarboxylic acids **8 a–8 c** in quantitative yields. These ω-hydroxycarboxylic acids showed sensitivity towards esterification. Oligomerization occurred spontaneously: even when stored at 4 °C, 15% of compound **8 b** was converted into oligomeric products in two weeks.

In search of simple cyclization procedures for the ω-hydroxycarboxylic acids **8 a–8 c**, we encountered an elegant procedure for the synthesis of macrocyclic esters by Bachrach [8]. Bachrach used metal salts, such as $SnCl_2$, $FeCl_3$, $MgCl_2$, $Co(NO_3)_2$ and $CoCl_2$ for the cyclization of glycol monosuccinates yielding the corresponding macrocyclic esters in good yields (>80% for 10 to 26 membered rings). The procedure was modified for the synthesis of 2-oxo-12-crown-4 (**2**) by performing the reaction at different temperatures, pressures and catalyst concentrations [9]. Additionally, the use of template salts MCl was investigated. The best results were obtained when the ω-hydroxycarboxylic acid **8 b**, the $CoCl_2$-catalyst (14 mol%) and the template salt CsCl (20 mol%) were heated in a kugelrohr apparatus for 16 h at 250 °C and at 18 mbar pressure. Purification of the distillate gave an isolated yield for **2** of 82% (vs. 60% without the use of CsCl). Templates other than CsCl were also tested: the purity of **2** in the distillate in five experiments showed the following sequence: no salt < LiCl < NaCl < KCl < CsCl. ^{1}H-NMR spectra of the crude distillates showed that the formation of the by-product 1,4-dioxanone was most prominent when LiCl was used. These results clearly prove the template-effect of the salts used. An additional advantage of the use of template salts as co-catalysts was the improved reproducibility of the cyclization reaction: yields remained constant as the reaction was scaled up (to 3.5 g of **8 b**).

The oxo-crown ether **3** was also synthesized following this method. The product was isolated in a yield of 32% when no template salt was used. Again, the yield increased when CsCl was added to the reaction mixture: an isolated yield of 59% was reached. Crown ether **1** was synthesized in an isolated yield of 29% (with a crude yield of 69% distillate), with CsCl being used as a template salt. For both **1** and **3** a temperature of 250 °C and a pressure of 0.05–0.1 mbar was applied.

In order to compare the $CoCl_2$-catalyzed cyclization to other cyclization procedures, several high dilution methods known for the cyclization of aliphatic ω-hydroxycarboxylic acids were tested on **8 b** and **8 c**. The methods of Corey [10], Mukaiyama [11] and Yamaguchi [12] gave products **2** and **3**, but isolated yields were in all cases lower than found for the $CoCl_2$/CsCl-catalyzed ring closure.

In conclusion, the $CoCl_2$-mediated ring closure of ω-hydroxycarboxylic acids **8 a–8 c** has been developed and optimized using MCl as template-salts. Therefore, a convenient route to oxo-crown ethers has been established. The Cs-salt template effect has been used extensively in the synthesis of other lactones [13] and seems of general use.

2.2. Polymerization of oxo-crown ethers 1–3

Analogous to the polymerization of other ether-lactones [5], the polymerization of oxo-crown ethers **1–3** was also conducted using $SnOct_2$ as catalyst [14]. Monomer/catalyst molar ratios of 50/1, 100/1 and 25/1 for **1**, **2** and **3** were applied, respectively. After reaction for typically 24–48 h at 130 °C, precipitation from dichloromethane in diethyl ether was carried out and polymers were obtained as yellow viscous oils. The molecular weights of the polymers varied from 7 to 11 kg/mol and dispersities between 1.5 and 1.9 were found. These data were based on SEC-measurements using polystyrene standards [15].

In earlier studies, it has been pointed out that alcohols – typically traces of water – are the main initiators in $SnOct_2$-

catalyzed lactone polymerizations [16]. To investigate the possibilities of (a) introducing specific endgroups to the polymer and (b) influencing the molecular weight of the polymer, a series of experiments was conducted in which 4-tert-butylbenzyl alcohol was added to the polymerization mixture of 2-oxo-12-crown-4 (**2**) and $SnOct_2$. A monomer/catalyst molar ratio of 50 and a polymerization temperature of 130 °C was chosen.

Table 1. $SnOct_2$-catalyzed polymerization of 2-oxo-12-crown-4 (**M**) with addition of tert-butylbenzyl alcohol (t-**BBA**). A molar monomer/catalyst-ratio of 50/1 and a polymerization temperature of 130 °C were used.

M/t-BBA-end-group molar ratio of crude polymer[a]	M/t-BBA-end-group molar ratio of precipitated polymer[b]	M_n calculated[c] [kg/mol]	M_n measured[d] [kg/mol]
45/1	85/1	16.2	4.7
34/1	57/1	10.8	4.0
20/1	46/1	8.7	3.2
10/1	24/1	4.6	2.8

[a] determined by ^{1}H-NMR, equals the M/t-**BBA** in the feed; [b] determined by ^{1}H-NMR; [c] calculated for the precipitated polymer; [d] based on SEC-analyses of the precipitated polymer using polyethylene oxide standards.

In the experiments, the monomer/alcohol molar ratio was varied from 45/1 to 10/1. SEC-analysis of the polymers after precipitation (see Table 1) showed that the molecular weight decreased as the monomer/tert-butylbenzyl-endgroup molar ratio decreased. The observed decrease in molecular weight was not proportional to the monomer/tert-butylbenzyl-endgroup ratio. At low monomer/tert-butylbenzyl-endgroup ratios, the calculated molecular weight and the measured molecular weight of the precipitated polymer were in reasonable agreement. This indicates that in this case the added alcohol is the main initiator in the polymerization. At higher monomer/tert-butylbenzyl-endgroup molar ratios, however, the measured molecular weights were significantly lower than the calculated molecular weights. This suggests that under these circumstances hydroxy contaminations (typically water) are the main initiators in polymerization. Initiation by $SnOct_2$ itself could not be excluded: in the ^{1}H-NMR spectra of the precipitated polymers small signals were observed that could be assigned to octanoate endgroups.

To further examine the $SnOct_2$-catalyzed polymerizations of oxo-crown ethers, the effect of temperature and catalyst concentration on the reaction rate, the molecular weight and the molecular weight distribution were studied. For this purpose two series of polymerizations of 2-oxo-12-crown-4 (**2**) at 100 °C, 115 °C, 130 °C and 145 °C were conducted. In the first series the monomer/catalyst molar ratio was 100/1, in the second series a ratio of 50/1 was applied.

Figure 3 shows the conversion vs. reaction time plots for both polymerization series (polymerization of oxo-crown ether **2** could be monitored by ^{1}H-NMR: at 3.55 and 3.80 ppm resonances of the monomer are isolated from resonances of the polymer). It is clear that at higher temperatures polymerization proceeds faster and that the monomer/catalyst ratio has a significant influence on the final conversion of polymerization. A minimum temperature of 115 °C and a minimum amount of catalyst are required to achieve complete conversion. The experiment shows that high

monomer/catalyst molar ratios – of for example 11 250 as applied in lactide polymerizations [16] and up to 5000 as applied in 1,5-dioxepan-2-one polymerizations [5] – cannot be applied to the polymerization of 2-oxo-12-crown-4.

During the second polymerization series ($M/SnOct_2$ = 50), samples were taken and analyzed by SEC. The polymer was detected using a refractometer and polyethylene oxide was used as a standard. The results of the measurements are depicted in Fig. 4.

In all chromatograms a high molecular weight peak as well as a low molecular weight peak are present. The reason for this bi-modal molecular weight distribution is not quite clear to us. The SEC-plots show that the low molecular weight peak gets smaller as conversion proceeds. A possible explanation is the formation of cyclic oligomers that transform into linear species as the polymerization proceeds [17].

The SEC-plots of the polymerization at 145 °C clearly show that degradation reactions take place at that temperature. When the chromatograms of the polymerization at 145 °C after 30 min (38% conversion), 4 h (nearly complete conversion) and 50.5 h (complete conversion) are compared, it is clear that the high molecular weight peak is shifted to lower molecular weights. This effect can – how- ever, less significantly – also be observed at 130 °C. The temperature has only a limited influence on the final molecular weight of the polymers obtained. The observed M_{top} of the polymers after 50.5 h reaction time hardly differs, when different temperatures are applied. Molecular weights (M_{top}) of 4.1, 4.7 and 5.0 kg/mol were measured for reaction temperatures of 115 °C, 130 °C and 145 °C, respectively.

3. Conclusion

The syntheses of the oxo-crown ethers 1–3 has been performed successfully using a powerful and simple cyclization technique: a template (CsCl) and Lewis-acid ($CoCl_2$) directed distillation of oxo-crown ethers from the ω-hydroxycarboxylic acid precursors. In contrast to the usual procedures, this method does not require large amounts of solvent. From Bachrach's work [8], it was already clear that this cyclization technique might be applicable to a variety of ω-hydroxycarboxylic acids. This work shows that this method can be improved by the use of well-chosen templates.

The polymerization of oxo-crown ethers with ring sizes of 12, 18 and 21 has been achieved using $SnOct_2$ as catalyst.
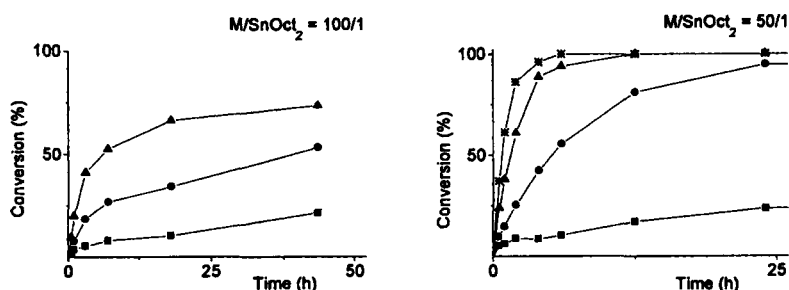
Fig. 3. Conversion vs reaction time plots of the 2-oxo-12-crown-4 (2) polymerizations at monomer/$SnOct_2$ molar ratios of 100/1 and 50/1 and at temperatures of 100 °C (square), 115 °C (circle), 130 °C (triangle) and 145 °C (star), respectively.
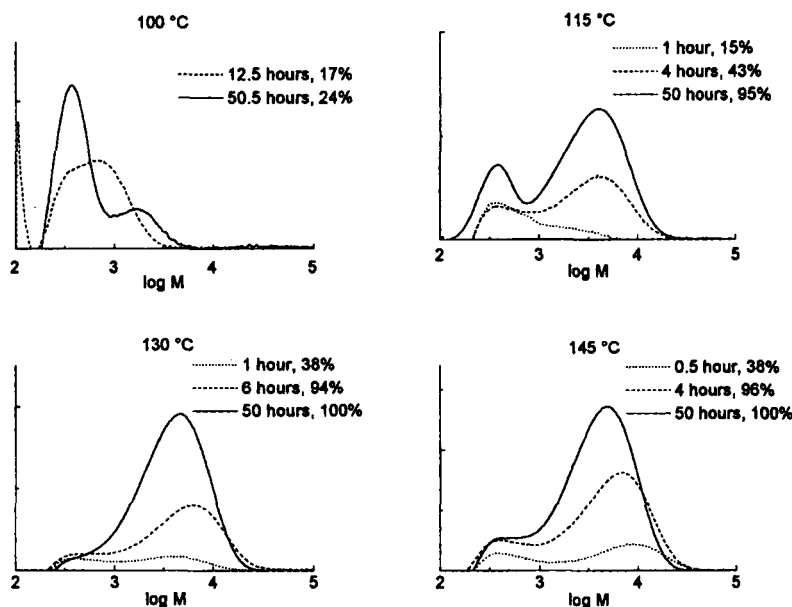
Fig. 4. SEC-plots of polymerizations of 2-oxo-12-crown-4 (2). Samples were taken at the reaction times indicated. Conversions at these reaction times are also indicated. A monomer/$SnOct_2$ molar ratio of 50/1 and temperatures of 100 °C, 115 °C, 130 °C and 145 °C were applied. Molecular weights were calculated with polyethylene oxide calibration standards. Vertical axes have arbitrary units.

The synthesis and polymerization of oxo-crown ethers

Polymers – viscous oils – with molecular weights of ca. 5 kg/mol and dispersities of ca. 1.8 are afforded. Analysis of the 2-oxo-12-crown-4 polymerization shows that a minimum temperature of 115 °C and a maximum monomer/catalyst molar ratio of (approximately) 100 are required to successfully perform these polymerizations. The molar ratio is much lower than usually applied to $SnOct_2$-catalyzed polymerizations of smaller lactones. The used polymerization technique facilitates the introduction of end-groups to the polymer: when an alcohol is mixed with monomer and catalyst, this alcohol acts as initiator and is thus introduced into the polymer as an endgroup. Investigations to use the new polymers in a variety of applications are in progress.

4. Experimental

General

Commercially available compounds employed in the syntheses were used without further purification, except stannous octanoate ($SnOct_2$) which was distilled in vacuo in a kugelrohr apparatus (0.3 mbar; 200–220 °C) and stored in a glove box. Solvents were dried if necessary and reactions were carried out in an inert atmosphere of dried argon or nitrogen. ^{1}H-NMR spectra were taken on an AM-400 Bruker spectrometer at 400 MHz or on a Gemini Varian 300 MHz spectrometer. TMS was used as internal standard. ^{13}C-NMR spectra were taken on the Bruker spectrometer at 101 MHz with the solvent as standard. SEC-analyses were conducted at 40 °C with stabilized THF as solvent and an eluent rate of 1 ml/min. The SEC apparatus was equipped with two Shodex KF 80-M (linear) columns and a differential refractive index detector (Waters 410). Molecular weights were determined with polyethylene oxide or polystyrene calibration standards. Infrared spectra were taken on a Perkin Elmer 1605 FTIR-spectrometer with wavenumbers between 4400 and 450 cm^{-1}. Electrospray MS (ES/MS) was performed on a Perkin Elmer/Sciex API-300 MS/MS (negative mode). GC/MS was performed on a HP 5790 GC with an OV-1 column and an HP 5970A MSD.

Kinetic experiments

All $SnOct_2$-catalyzed polymerizations of 2 referred to in the time-conversion plots (Fig. 3), the SEC-plots (Fig. 4) and in the polymerization series with added 4-tert-butylbenzyl alcohol were conducted in silylated glassware with distilled monomer and distilled $SnOct_2$. In a glove box a 0.158 M $SnOct_2$ toluene solution, distilled monomer and (if required) pure 4-tert-butylbenzyl alcohol were brought together in silylated Schlenk flasks. Thereafter, the solutions were stirred in an inert atmosphere of dried argon at the polymerization temperature. The toluene was not removed in a separate step, because the amount of this solvent was small relative to the amount of monomer. When samples were taken from the reaction mixtures during polymerization, this was done either in a glove box or under a strong argon flow. Conversions of the polymerizations were determined by ^{1}H-NMR-analysis of the samples taken. Samples of the NMR-tubes were used in the SEC measurements.

{2-(2-Benzyloxy-ethoxy)-ethoxy}-acetic acid (7a)

A solution of 5 a (15.0 g; 76.4 mmol) and tBuOK (17.14 g; 152.8 mmol) in dry dimethylformamide (DMF) was stirred at room temperature for 1 h under an argon atmosphere. The solution turned brown. Bromoacetic acid (11.23 g; 76.43 mmol) in 50 ml of dry DMF was added dropwise, while the solution was cooled in an ice bath. A suspension was formed immediately. After all the bromoacetic acid was added, the ice bath was removed and the solution was stirred for another hour. DMF was evaporated and the residue was dissolved in 100 ml of a 1 M NaOH solution and stirred for an hour. The starting product 5 a was removed by extraction of the aqueous layer with dichloromethane. The aqueous layer was then brought to a pH of 2 with a HCl solution and extraction with dichloromethane yielded crude product, which was contaminated with tert-butoxy acetic acid. This contamination was removed by coevaporation with tetralin. Distillation in a kugelrohr apparatus (200–225 °C; 0.05 mbar) yielded the pure title compound as a viscous oil in a yield of 55% (10.61 g). ^{1}H-NMR (CDCl$_3$): δ 7.4–7.2 (5H, m), 4.56 (2H, s), 4.18 (2H, s), 3.8–3.55 (8H, m). ^{13}C-NMR (CDCl$_3$): δ 173.7, 137.7, 128.1, 127.6, 127.4, 72.9, 70.8, 70.3, 70.1, 69.0, 68.1. FTIR (KBr, cm^{-1}): 3030, 2871, 1744, 1496, 1454, 1354, 1246, 1206, 1119, 1026, 931, 883, 852, 740, 699. These data are in agreement with the data published in an earlier report [18].

{2-(2-Hydroxy-ethoxy)-ethoxy}-acetic acid (8 a)

Compound 7 a (7.35 g; 26 mmol) was dissolved in a mixture of 100 ml dioxane, 5 ml water and a few drops of concentrated hydrochloric acid. Pd/C (10%) (0.10 g) was added to this solution and hydrogenation under 50 psi H$_2$-overpressure for 2.5 h gave complete debenzylation. The suspension was filtrated and the filtrate was concentrated in vacuo to yield the title product as a viscous oil that was slightly contaminated with oligomers as a result of esterification. Yield: 4.0 g (93%). ^{1}H-NMR (CDCl$_3$): δ 7.0 (2H, bs), 4.17 (2H, s), 3.8-3.55 (8H, m). ^{13}C-NMR (CDCl$_3$): δ 172.9, 72.2, 70.7, 70.0, 68.1, 61.1. HRMS Calcd. 164.0685. Found 164.0685.

2,11-Dioxo-18-crown-6 (1)

CoCl$_2$·6H$_2$O (155 mg; 0.65 mmol) and CsCl (166 mg; 0.99 mmol) were added to compound 8 a (1.023 g; 6.23 mmol). The deep-blue mixture was heated to 250 °C in a kugelrohr apparatus at 0.05 mbar for 12 h. The collected distillate solidified upon cooling. The crude product (0.627 g) was dissolved in acetonitrile and filtered over a short column (alumina, acetonitrile, R_f = 0.82). The filtrate was concentrated to give the title compound as a white solid. Yield: 0.262 g (29%). ^{1}H-NMR (CDCl$_3$): δ 4.37 (4H, s), 4.32 (4H, m), 3.78 (4H, m), 3.71 (8H, m). ^{13}C-NMR (CDCl$_3$): δ 170.4, 72.1, 69.9, 69.0, 68.5, 63.6. Calcd 292.29. Found GC/MS 292 (1.6% abundance).

[2-{2-(2-Benzyloxy-ethoxy)-ethoxy}-ethoxy]-acetic acid (7 b)

Compound 5 b was coevaporated two times with toluene. A solution of 5 b (100.0 g; 416.7 mmol) in 100 ml dry DMF

was added to a solution of 'BuOK (93.52 g; 833.3 mmol) in 150 ml dry DMF. The mixture turned from yellow to dark brown and was stirred for 2 h at room temperature under an argon atmosphere. Bromoacetic acid (58.48 g; 416.7 mmol) in 100 ml dry DMF was added dropwise over a period of 1 h, while the mixture was cooled in an ice bath. On addition of bromoacetic acid, a suspension was immediately formed. The mixture was stirred overnight. DMF was evaporated and the residue was dissolved in 1 liter of a 1 M NaOH-solution. The deep orange aqueous layer was extracted with dichloromethane to remove all the unreacted 5 b. (The dichloromethane layers were collected, dried with $MgSO_4$, filtered and concentrated to recover 15.15 g of 5 b.) The aqueous layer was brought to a pH of 2 with concentrated HCl and thereafter extracted with dichloromethane to yield crude product. The *tert*-butoxy acetic acid contamination was removed by coevaporation with tetralin. The title compound was obtained as a brown viscous oil. Yield 93.83 g (76%). ^{1}H-NMR ($CDCl_3$): δ 7.4–7.2 (5H, m), 4.55 (2H, s), 4.1 (2H, s), 3.75–3.55 (12H, m). ^{13}C-NMR ($CDCl_3$): δ 173.2, 137.7, 128.0, 127.5, 127.3, 72.8, 70.7, 70.2, 70.1 (3C), 69.0, 68.1. FTIR (KBr, cm^{-1}): 3030, 2871, 1755, 1496, 1453, 1350, 1248, 1205, 1110, 1027, 944, 853, 740, 700. HRMS Calcd. 298.1416. Found 298.1411.

[2-{2-(2-Hydroxy-ethoxy)-ethoxy}-ethoxy]-acetic acid (8 b)

Compound 7 b (8.0 g; 26.8 mmol) was dissolved in a mixture of 100 ml dioxane, 5 ml water and a few drops of concentrated HCl. Pd/C (10%) (0.1 g) was added and the mixture was shaken under 50 psi H_2-overpressure for 7 h. After 4 h new Pd/C was added. The suspension was filtered and concentrated in vacuo. Compound 8 b was obtained as a clear oil (97%, 5.35 g). ^{1}H-NMR ($CDCl_3$): δ 7.6–7.1 (2H, bs), 4.11 (2H, s), 3.75–3.5 (12H, m). ^{13}C-NMR ($CDCl_3$): δ 172.3, 72.3, 70.7, 70.5, 70.1, 70.0, 68.7, 61.5.

2-Oxo-12-crown-4 (2)

$CoCl_2 \cdot 6H_2O$ (160 mg; 0.67 mmol) and CsCl (160 mg; 0.95 mmol) were added to compound 8 b (1.08 g; 5.19 mmol). The deep blue mixture was heated to 250 °C at 18 mbar in a kugelrohr apparatus for 16 h. A clear oil was distilled. The crude product contained trace amounts of 1,4-dioxanone and dimer and was purified by column chromatography (silica, EtOAc, R_f = 0.33) to yield the title compound as a clear oil. Yield: 0.81 g (82%). ^{1}H-NMR ($CDCl_3$): δ 4.35 (2H, m), 4.15 (2H, s), 3.8 (4H, m), 3.7 (2H, m), 3.65 (2H, m), 3.55 (2H, m). ^{13}C-NMR ($CDCl_3$): δ 171.0, 72.0, 71.4, 71.3, 70.2, 69.8, 68.8, 63.4. Calcd 190.20. Found GC/MS 190 (<1% abundance). HRMS Calcd. 190.0841. Found 190.0856. *2,14-dioxo-24-crown-8 (dimer):* ^{1}H-NMR ($CDCl_3$): δ 4.35 (4H, m), 4.25 (4H, dd), 3.8–3.7 (12H, m), 3.65 (8H, s). ^{13}C-NMR ($CDCl_3$): δ 170.7, 71.0, 70.9, 70.7, 70.5, 68.9, 68.8, 63.7. R_f(EtOAc, silica) = 0.10. Calcd 380.40. Found GC/MS 380 (<1% abundance). Clear oil. *1,4-dioxanone (byproduct):* ^{1}H-NMR ($CDCl_3$): δ 4.52 (2H, m), 4.4 (2H, s), 3.9 (2H, m). ^{13}C-NMR ($CDCl_3$): d 166.5, 68.5, 66.2, 62.5. Calcd 102.09. Found GC/MS 102 and 103 (27.8% and 1.6% abundance).

Monobenzyl hexaethylene glycol (5 c)

A solution of *t*BuOK (6.25 g; 56.1 mmol) in *t*BuOH (45.4 g) was added dropwise to hexaethylene glycol (4 c) (31.41 g; 111.2 mmol) under an argon atmosphere. The mixture was stirred at room temperature for 2 h and thereafter concentrated. The resulting dark-brown viscous oil was taken up in 25 ml of dry dioxane. Benzyl chloride (7.0 g; 55.3 mmol) was added dropwise at room temperature and the mixture was heated at 55 °C overnight. The reaction mixture was filtered and the residue washed with dichloromethane. The filtrate was concentrated and dissolved in acidic water (pH = 2). The water layer was extracted with diethyl ether to remove the byproduct dibenzyl hexaethylene glycol. Further extraction with dichloromethane provided the crude title compound, which was purified by column chromatography (silica, dichloromethane/MeOH = 19/1, R_f = 0.28) to yield a clear oil (14.47 g, 70%). ^{1}H-NMR ($CDCl_3$): δ 7.4–7.2 (5H, m), 4.55 (2H, s), 3.8–3.5 (24H, m), 2.8 (1H, bs). ^{13}C-NMR ($CDCl_3$): δ 138.1, 128.2, 127.6, 127.4, 73.0, 72.4, 70.4 (8C), 70.2, 69.3, 61.5.

FTIR (KBr, cm^{-1}): 3381, 3030, 2870, 1495, 1455, 1351, 1296, 1249, 1206, 1143, 1100, 948, 738, 700.

[2-{2-(2-[2-{2-(2-Benzyloxy-ethoxy)-ethoxy}-ethoxy]-ethoxy)-ethoxy}-ethoxy]-acetic acid t-butyl ester (6 c)

To a stirred solution of 5 c (19.2 g; 52 mmol) in 80 ml *t*BuOH, *t* BuOK (5.80 g, 52 mmol) was added in small portions. The mixture was stirred for 1 h at room temperature. *t*Butyl-bromoacetate (18.12 g, 93 mmol) was added dropwise, while the solution was cooled in a water bath. Upon addition a suspension was immediately formed. The mixture was stirred for a few hours. *t* BuOH was evaporated, the residue was brought in water and extraction with dichloromethane was carried out. The collected organic layers were concentrated and the crude product was purified by column chromatography (silica, EtOAc, R_f = 0.32). The *t*-butyl ester (6 c) was obtained as a clear oil (18.54 g, 70%). The product was pure according to NMR and TLC. ^{1}H-NMR ($CDCl_3$): δ 7.4-7.3 (5H, m), 4.55 (2H, s), 4.02 (2H, s), 3.8–3.55 (24H, m), 1.45 (9H, s). ^{13}C-NMR ($CDCl_3$): δ 170.1, 138.2, 128.2, 127.6, 127.4, 81.7, 73.1, 70.6, 70.5 (10C), 69.3, 69.0, 28.0. FTIR (KBr, cm^{-1}): 2869, 1747, 1454, 1368, 1227, 1144, 1110, 943.

[2-{2-(2-[2-{2-(2-Benzyloxy-ethoxy)-ethoxy}-ethoxy]-ethoxy)-ethoxy}-ethoxy]-acetic acid (7 c)

Trifluoroacetic acid (23.1 ml; 0.3 mol) was added to compound 6 c. The mixture was stirred for 1 h at room temperature under an argon atmosphere. The mixture was concentrated in vacuo and the residue was dissolved in 200 ml dry diethyl ether. The solution was added to 450 ml water, which was kept at a pH of 12 by simultaneous addition of a 0.4 M NaOH solution. The aqueous layer was washed with dichloromethane and diethyl ether to remove contaminations. After the aqueous layer had been brought to a pH of 2, it was extracted with dichloromethane. The dichloromethane layers were collected, dried with $MgSO_4$ and concentrated to yield 7 c as a viscous oil. Yield: 8.60 g (86%). ^{1}H-NMR ($CDCl_3$): δ 9.8 (1H, bs), 7.3–7.15 (5H, m), 4.55 (2H, s), 4.05 (2H, s), 3.75 (2H, m), 3.7–3.5 (22H, m). ^{13}C-NMR

(CDCl$_3$): δ 172.4, 138.1, 128.2, 127.7, 127.5, 73.1, 71.2, 70.5–70.4 (9C), 70.3, 69.3, 68.7. FTIR (KBr, cm^{-1}): 3467, 2872, 1740, 1455, 1351, 1297, 1249, 1201, 1112, 950, 849, 741. Calcd C 58.59 H 7.96: Found C 58.36 H 7.57. Calcd 430.39. Found ES/MS (negative mode) 429.

[2-{2-(2-[2-{2-(2-Hydroxy-ethoxy)-ethoxy}-ethoxy]-ethoxy)-ethoxy}-ethoxy]-acetic acid (8 c)

Compound 7 c (13.0 g, 30 mmol) was dissolved in 100 ml dioxane and Pd/C (10%) was added. The mixture was shaken for 8 h under a 30 psi H$_2$-overpressure. The catalyst was removed by centrifugation, the solvent was evaporated in vacuo and the title compound was obtained as a yellowish oil. Yield: 10.0 g (97%). ^{1}H-NMR (CDCl$_3$): δ 7.0 (2H, bs), 4.15 (2H, s), 3.8–3.5 (24H, m). ^{13}C-NMR (CDCl$_3$): δ 172.4, 72.3, 70.9, 70.4–70.3 (7C), 70.2, 70.1, 68.5, 61.4. Calcd 340.37. Found ES/MS (negative mode) 339.

2-Oxo-21-crown-7 (3)

CoCl$_2$·6H$_2$O (90 mg; 0.38 mmol) and CsCl (50 mg; 0.30 mmol) were added to 8 c (0.91 g; 2.59 mmol). The blue solution was heated to 250 °C at 0.08 mbar in a kugelrohr apparatus for 8 h. A clear oil was distilled. Column chromatography (silica, EtOAc/acetonitrile (1 : 1), R_f= 0.2–0.3) gave the title compound in a yield of 59% (0.51 g). ^{1}H-NMR (CDCl$_3$): δ 4.3 (2H, m), 4.25 (2H, s), 3.75–3.6 (22H, m). ^{13}C-NMR (CDCl$_3$): δ 170.7, 71.3, 71.0–70.4 (9C), 68.9, 68.7, 63.7. FTIR (KBr, cm^{-1}): 2869, 1753, 1452, 1350, 1203, 1122, 1042, 946, 850, 751. Calcd 322.36. Found MS (positive CI with NH$_3$) 322 and 340 (ammonium complex of 3).

SnOct$_2$-catalyzed polymerization of 1,4,7,10,13,16-hexaoxacyclo-octadecan-2,11-dione (1), typical procedure

Compound 1 (0.20 g; 0.68 mmol) was transferred to a glove box where 87 µl of a 0.158 M solution of SnOct$_2$ in dry toluene was added to the monomer. Thereafter, polymerization was carried out under an inert atmosphere of dry argon at 130 °C. The polymerization was stopped after 20 h (100% conversion). The crude polymer was dissolved in a small amount of dichloromethane and precipitated in diethyl ether. After the ether was decanted, the polymer was again dissolved in a small amount of dichloromethane. Precipitation in hexane yielded the polymer as a yellowish sticky oil. Yield: 0.17 g (85%). *Poly-(1,4,7,10,13,16-hexaoxacyclo-octadecan-2,11-dione)*: ^{1}H-NMR (CDCl$_3$): δ 4.30 (2H, m), 4.17 (2H, s), 3.80–3.60 (6H, m). ^{13}C-NMR (CDCl$_3$): δ 170.3, 70.8, 70.5, 68.9, 68.5, 63.8. SEC-analysis: M_n = 7.5 kg/mol, M_w/M_n = 1.7 (polystyrene calibration standards were used).

SnOct$_2$-catalyzed polymerization of 1,4,7,10-tetraoxacyclododecan-2-one (2), typical procedure

Compound 2 was distilled in vacuo (0.005 mbar; 80 °C) and immediately transferred to a glove box. There, 2 (2.00 g; 10.5 mmol) was brought in a 10 ml Schlenk flask which

had previously been silylated. A 0.158 M solution of SnOct$_2$ in toluene (1.33 ml) was added to the monomer. The Schlenk flask was transferred out of the glove box and the toluene was evaporated in vacuo. Thereafter, the polymerization was conducted at 130 °C under an inert atmosphere of dry argon. The reaction was stopped after 20 h (100% conversion). The crude polymer was dissolved in a minimum amount of dichloromethane and precipitated in diethyl ether. The diethyl ether was decanted and the polymer was again dissolved in dichloromethane and precipitated in hexane. The polymer was obtained as a clear sticky oil. Yield: 1.77 g (89%). *Poly-(1,4,7,10-tetraoxacyclododecan-2-one)*: ^{1}H-NMR (CDCl$_3$): δ 4.35–4.29 (2H, m), 4.19 (2H, s), 3.77–3.60 (10H, m). ^{13}C-NMR (CDCl$_3$): δ 170.4, 70.9, 70.5 (3C), 68.9, 68.4, 63.8. SEC-analysis: M_n = 9.0 kg/mol, M_w/M_n = 1.87 (polystyrene calibration standards were used).

SnOct$_2$-catalyzed polymerization of 1,4,7,10,13,16,19-heptaoxacycloheneicosan-2-one (3), typical procedure

Compound 3 (0.20 g; 0.62 mmol) was dried by adding 50 ml of dry toluene and heating the solution under reflux for 16 h in a Soxhlet extraction apparatus with 12 g 3 Å molecular sieves in the thimble, under a dry argon atmosphere. The toluene was evaporated in vacuo. A 0.0248 M solution of SnOct$_2$ in dry hexane was prepared in a glove box and 1 ml of this solution was added to the monomer (M/SnOct$_2$ = 25). Dry toluene was added to collect all monomer at the bottom of the flask. The mixture was stirred at 40 °C for one hour under a strong argon atmosphere to evaporate all solvent. Polymerization was performed by heating the mixture to 130 °C under a dry argon atmosphere. The polymerization was stopped after 144 h (93% conversion). The crude polymer was dissolved in a minimum amount of dichloromethane and precipitated in diethyl ether. The ether was decanted and the polymer was again dissolved in dichloromethane. Precipitation in hexane yielded the polymer as a brownish sticky oil. *Poly-(1,4,7,10,13,16,19-heptaoxacycloheneicosan-2-one)*: ^{1}H-NMR (CDCl$_3$): δ 4.31–4.28 (2H, m), 4.18 (2H, s), 3.64–3.37 (22H, m). ^{13}C-NMR (CDCl$_3$): δ 170.4, 70.9, 70.5 (9C), 68.9, 68.5, 63.8. FTIR (KBr, cm^{-1}): 3484 (w), 2868, 1959, 1752, 1455, 1350, 1286, 1124, 1042, 950, 853, 724, 578. SEC-analysis: M_n = 11.4 kg/mol, M_w/M_n= 1.9 (polystyrene calibration standards were used).

Polycondensation of 8 a

Compound 8 a (0.22 g; 1.35 mmol) was stirred at 200 °C under a strong argon atmosphere for 4 h. Thereafter, it was heated in vacuo (0.2 mbar) for another 3 h at 225 °C. Poly-(1,4,7,10,13,16-hexaoxacyclo-octadecane-2,11-dione) was obtained in this way as a brownish sticky oil. The molecular weight was determined by SEC-analysis (M_n = 7.9 kg/mol, M_w/M_n = 2.0).

Polycondensation of 8 b

Compound 8 b (0.22 g; 1.06 mmol) was stirred under a nitrogen atmosphere for 4 h. Thereafter, it was heated in vacuo (0.01 mbar) for another 4 h at 200 °C. Poly-(1,4,7,10-

tetraoxacyclododecan-2-one was obtained in this way as a brown sticky oil. Yield: 0.188 g (92.7%). The molecular weight was determined by SEC-analysis ($M_n = 4.9$ kg/mol, $M_w/M_n = 1.7$).

Acknowledgement

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[17] A second explanation in accordance with the observed behavior is the following. Initiation and propagation take place via a coordination polymerization mechanism, see Ref. [16] (the SnOct₂-catalyst is attached to one end of the oligomer). However, detachment of the catalyst from the polymer-end takes place at a speed comparable to the speed of initiation and propagation. This will result in short oligomers (typically 3 monomers in length) that can polymerize via polycondensation (giving longer oligomers of 6 monomers in length). If the speed of polycondensation is lower than the speed of initiation and propagation, these short oligomers will accumulate. Moreover, oligomers of 4 and 5 monomers in length will be statistically 'absent'. Polycondensations of compounds 8 a and 8 b gave polymers with molecular weights of $M_n = 7.9$ kg/mol and $M_n = 4.9$ kg/mol and dispersities of 2.0 and 1.7, respectively. The results of these simple polycondensations do not differ enormously from the results of the SnOct₂-catalyzed polymerizations of the oxo-crown ethers 1 and 2.

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