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Synthesis of aliphatic poly(ester-amide)s containing uniform bisamide-bisester blocks

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SUMMARY: Aliphatic copoly(ester-amide)s containing short, uniform amide blocks were synthesized from dimethyl adipate, 1,4-butanediol and dimethyl 7,12-diaza-6,13-dioxo-1,18-octadecanedioate by polycondensation in the melt using tetrabutyl(orthotitanoate) as a catalyst. The bisamide blocks were randomly distributed as was shown by ^{1}H NMR. M_w values of around 50 000 g·mol^{-1} and molecular weight distributions M_w/M_n close to 2 were obtained for all poly(ester-amide)s.

Introduction

A major challenge in the design and development of compostable polymers is the combination of useful thermal and mechanical properties and complete biodegradability. Segmented block-copolymers may have considerable advantages above completely random copolymers$^{1)}$. In such segmented copolymers the properties of the two homopolymers are preserved to some extent due to phase separation on a microscale level. Phase separation can be achieved by crystallization of one of the segments and can be enhanced by incorporating uniform blocks in the copolymer. In general, the non-crystallizable segments form an amorphous matrix in which the crystallizable blocks are present as lamellae and act as physical cross-links. We have used this strategy by designing segmented block-copolymers comprising hydrolytically and/or enzymatically cleavable bonds in the main chain.

Previously described poly(ester-amide)s based on N,N'-1,4-butanediyl-bis[6-hydroxy-hexanamide] monomers, dimethyl adipate and 1,4-butanediol$^{2)}$ showed useful processing properties. These polymers rapidly degraded in soil and were completely mineralized after about 60 days depending on the polymer composition using aquatic Sturm tests. Moreover the polymers showed a good micro-scale phase separation between the crystalline and the amorphous phase and even nanoscale phase separation between ester and amide sequences

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in the melt was observed. Rapid crystallization from the melt was obtained over a broad composition range.

A major drawback in the preparation of these copoly(ester-amide)s is the difficulty to maintain stoichiometric reaction conditions especially at higher amide content. As a result only materials with moderate molecular weights could be prepared. To overcome this drawback without the loss of the described favourable properties the synthesis of such poly(ester-amide)s was based on uniform bisester-bisamide blocks. It is expected that stoichiometric conditions can be maintained at a higher degree of polymerization when excess volatile aliphatic diols in the initial monomer mixture are used. Here the synthesis of the amide containing monomers as well as copoly(ester-amide)s prepared by melt polycondensation of these monomers, dimethyl adipate, and 1,4-butanediol are described.

Experimental

Materials

Glutaric anhydride, dimethyl adipate, tetrabutylorthotitanoate ($Ti(OBu)_4$), 1,4-butanediamine, 1,4-butanediol and 1,2-ethanediol were obtained from Merck, Darmstadt. Deuterated solvents DMSO-d6, D_2O, $CDCl_3$ were obtained from Merck, Darmstadt. TFA-d1 was obtained from Acros, Belgium. All solvents used were of analytical grade.

Methods

^1H and ^{13}C NMR spectra were recorded at room temperature on a Bruker AC 250 operating at 250 MHz (^1H) or 62.5 MHz (^{13}C) using chloroform-d_1, DMSO-d_6, D_2O or trifluoroacetic acid-d_1 as solvents. The number-average degree of polymerization of the prepolymers was determined from ^1H NMR spectra by end group analysis with the assumption that only alcohol endgroups were present.

Elemental analysis and water content measurements were performed at the Laboratory of Chemical Analysis of the University of Twente.

Gel permeation chromatography (GPC) was used to determine molecular weights and molecular weight distributions (M_w/M_n). A Waters 6000A GPC apparatus equipped with four Waters µStyragel (500, 103, 104, 105 Å pore diameter) columns was used, combined with a H502 viscometer detector (Viscotek Corp.) for determination of absolute values of molecular weights. Polymers were dissolved in chloroform (1.0 wt. %) and elution was performed at 30 °C at a flow rate of 1.6 cm^3/min using $CHCl_3$ as eluent.

dimethyl 6,11-diaza-5,12-dioxo-1,16-hexadecanedioate (1b)

To a solution of glutaric anhydride (10.84 g, 0.095 mol) in 45 cm^3 THF:MeOH (2:1 v/v), a solution of 1,4-butanediamine (4.18 g, 0.0475 mol) in 20 cm^3 THF was added dropwise. After 8 hrs, the reaction mixture was cooled at -20 °C where-upon large crystals were formed. The precipitate was filtered off and dried overnight at 30°C in vacuo. The obtained product (**1a**) was characterized with 1H- and 13C-NMR and elemental analysis. 1a (10.0 g) was dissolved in 150 cm^3 refluxing methanol (T=95°C) and 1 cm^3 concentrated sulphuric acid was added. After 10 hrs, the reaction mixture was cooled to -20°C where-upon the product crystallized. Product (**1b**) was filtered and dried overnight at 30°C in vacuo.

^{1}H-NMR (1a) (DMSO-d_6): $\underline{H}O(O)C$: δ=12.02 (bs, 2H), $HO(O)CC\underline{H}_2CH_2$: δ=2.20 (t,4H), $HO(O)CCH_2C\underline{H}_2CH_2$: δ=1.75(p, 4H), $HO(O)CCH_2CH_2C\underline{H}_2$: δ=2.10 (t,4H), $C\underline{H}_2C(O)N(H)$: δ=2.05 (t, 4H), $C(O)N(\underline{H})$: δ=7.80 (bs, 2H), $N(H)C\underline{H}_2CH_2$: δ=3.08 (dt,); $N(H)CH_2C\underline{H}_2$: δ =1.42 (p, 4H) (1b) (DMSO-d_6): $C\underline{H3}O(O)C$: δ=3.6 (bs, 6H), $CH_3O(O)CC\underline{H}_2CH_2$: δ=2.1(t,4H), $CH_3O(O)CCH_2C\underline{H}_2$: δ=1.7 (p, 4H), $C\underline{H}_2C(O)N(H)$: δ=2.3 (t, 4H), $C(O)N(\underline{H})$: δ=7.8 (bs, 2H), $N(H)C\underline{H}_2CH_2$: δ =3.0 (dt,4H); $N(H)CH_2C\underline{H}_2$: δ=1.4 (p,4H)

dimethyl 7,12-diaza-6,13-dioxo-1,18-octadecanedioate (2)

Dimethyl adipate (233.85 g, 1.34 mol) and 1,4-butanediamine (11.83 g, 0.134 mol) were mixed at T=50°C., whereafter $Ti(OBu)_4$ (0.1 g, 0.2 wt %) was added. Methanol was distilled off at this temperature during 4 hours. During the next 4 hrs the temperature was increased every half hour with 25°C to a final temperature of 150°C. The melt was then allowed to cool to room temperature. A white solid product crystallizes during cooling and was filtered off. The product is then dissolved in warm chloroform (T=50°C). Non-soluble material was removed by filtration. and chloroform was evaporated under reduced pressure. The crude product was washed three times with cold THF to remove remaining dimethyl adipate. The obtained product (2) was then dried at 30°C in vacuo. ^{1}H NMR (DMSO-d_6): $C\underline{H}_3O(O)C$: d =3.8 (bs, 6H), $HO(O)CC\underline{H}_2CH_2$: δ =2.2(t,4H), $CH_3O(O)CCH_2C\underline{H}_2CH_2$: δ =1.48

(bs, 4H), $CH_3O(O)CCH_2CH_2C\underline{H}_2$: δ =1.48 (bs, 4H), $C\underline{H}_2C(O)N(H)$:δ=2.29 (t, 4H), $C(O)N(\underline{H})$: δ =7.78 (bs, 2H), $N(H)C\underline{H}_2CH_2$: δ =2.99 (dt, 4H); $N(H)CH_2C\underline{H}_2$: δ =1.35 (p, 4H)

Typical procedure for the preparation of 5 g (0.0084 mol) of a polyesteramide containing 33.3 mol % monomer **2**. The reaction was carried out in a glass reactor, with inlet for N_2 and a mechanical stirrer. To a mixture of 1.46 g (0.0084 mol) dimethyl adipate, 3.11 g (0.0084 mol) monomer 2 and 3.011 g (0.0168) 1,4-butanediol, 190 µl of a $Ti(OBu)_4$ solution (0.05 g/cm^3 in toluene) were added. The polymerization mixture was heated to 175°C and methanol was distilled off during 2-3 hrs under a constant nitrogen flow. Under reduced pressure (5 mbar) the temperature was raised to 190°C, whereafter the pressure was further reduced to 0.08-0.1 mbar. Excess 1,4-butanediol was distilled off during 2 hrs. The white/pale yellow viscous melt was cooled and characterized.

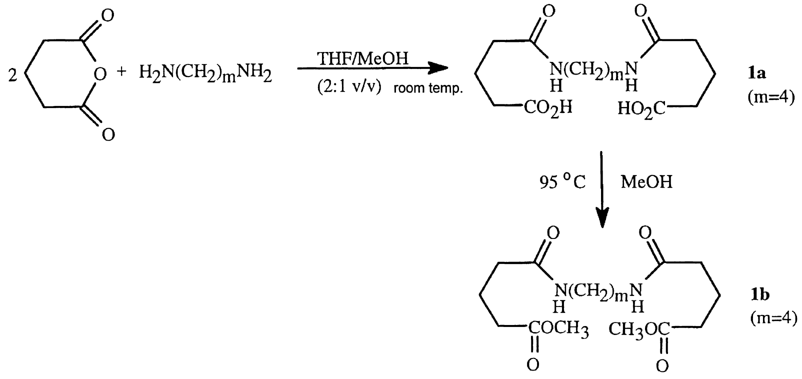
Results and discussion

Symmetrical bisacid or bisester amides were synthesized via 2 different routes. First, the ring-opening of cyclic dicarboxylic anhydrides with α,ω-diamines and subsequent esterification of the bisacid-diamide formed was investigated.

Imming and Yang3) reported on such a ring-opening reaction using different solvents and various temperatures. In chloroform and at low temperatures zwitterionic amides were obtained which precipitated from the reaction mixture. In protic solvents like ethanol two moles of anhydride react with one mol of diamine. These 2:1 products however, precipitated as their diammonium salts.

It was observed that reaction conditions which guaranteed a large excess of glutaric anhydride present avoided the formation of bis-ammonium salts between the formed bisacid-diamide and diamine. Therefore, the amount of diamine was slowly added to the anhydride solution in order to maintain an excess of anhydride, and the diacid **1a** was obtained in 91 % yield (Scheme 1). The diacid **1a** was subsequently converted into the bisester-diamide **1b** using methanol and sulfuric acid.

Although the described ring-opening reaction is very efficient, it is limited to a few commercially attractive cyclic anhydrides, i.e. succinic anhydride and glutaric anhydride. A cyclic anhydride like adipic anhydride in this respect is hardly interesting from our point of view due to its very high cost-prize. Therefore, an alternative route, the aminolysis reaction of linear aliphatic bisesters or bisacid chlorides with a,w-diamines, was investigated

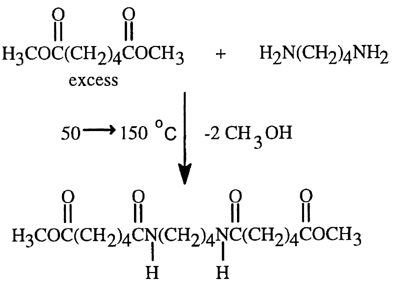


Scheme 1: The synthesis of dimethyl 6,11-diaza-5,12-dioxo-1,16-hexadecanedioate

Several authors have reported on the synthesis of oligoamides through aminolysis of linear diesters or diacid chlorides with α,ω-diamines. In different papers both Cowell[4)] and Zahn and Lauer[5)] described synthesis of linear oligoamides in moderate yields from adipic acid dichlorides or monoethylester acid chlorides and various diamines in pyridine. Astargo et al.[6)] prepared symmetrical 2:1 adducts in moderate yields from non-activated diesters and linear diamines using the lipase *Candida antartica* as a catalyst in non-aqueous media. Recently, Jouffret and Madec[7)] synthesized the 1:1 adduct of dimethyl adipate and 1,6-diaminohexane in high yield in the melt by careful control of the reaction temperature. The 1:1 adduct was used as a precursor for nylon-6,6.

In order to avoid the use of hazardous reactants such as acid chlorides and toxic solvents such as pyridine we attempted to synthesize the 2:1 adducts from dimethyl adipate and 1,4-butane diamine in the melt (Scheme 2). An excess dimethyl adipate was used to avoid oligomerization. The reaction was initially performed at 50°C. The 1:1 adduct is formed at this temperature and may slowly precipitate. When the formation of methanol decreased the temperature was raised stepwise to 150°C to induce further aminolysis. The precipitated 1:1

adduct melts again at 100°C and after a total reaction time of 8 hrs the crude product **2** was formed. The crude product obtained contained some insoluble oligomers (1-2 wt %) and unreacted dimethyl adipate. The oligomers could easily be removed by selective dissolution of the product and dimethyl adipate in warm chloroform. The product was then washed with THF to remove dimethyl adipate.



$$\underset{\text{excess}}{H_3CO\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{O}{\overset{\|}{C}}OCH_3} + H_2N(CH_2)_4NH_2 \xrightarrow[-2\,CH_3OH]{50 \rightarrow 150\,^{\circ}C} H_3CO\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{O}{\overset{\|}{C}}\underset{H}{\underset{|}{N}}(CH_2)_4\underset{H}{\underset{|}{N}}\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{O}{\overset{\|}{C}}OCH_3$$

2

Scheme 2: Aminolysis scheme of 1,4-butanediamine and dimethyl adipate

The purified product **2** was obtained in 71 % yield and was soluble in polar solvents like DMSO, $CHCl_3$ and warm water, but insoluble in THF, toluene and hexane. The ^1H NMR and ^{13}C NMR spectra (Fig. 1) and elemental analysis revealed the correct structure and purity of the bisester amide monomer to be used in the polycondensation reactions.

Poly(ester-amide)s were synthesized through melt polycondensation of dimethyl adipate, 1,4 butanediol and monomer **1b** or **2**, using $Ti(OBu)_4$ as a catalyst (Scheme 3). No diacid monomers were used to prevent extensive acidolysis during polymerization[6]. The results for the homo- and copolymers based on monomer **1b** revealed that although methanol and 1,4-butanediol were distilled off during polycondensation no significant increase of the melt viscosity was observed during 5 to 7 hrs reaction at reduced pressure. Yields were low and 1H-NMR analysis of the products showed the disappearance of the amide protons and a downfield chemical shift of the α-methylene protons from δ 3.25 to δ 3.71.

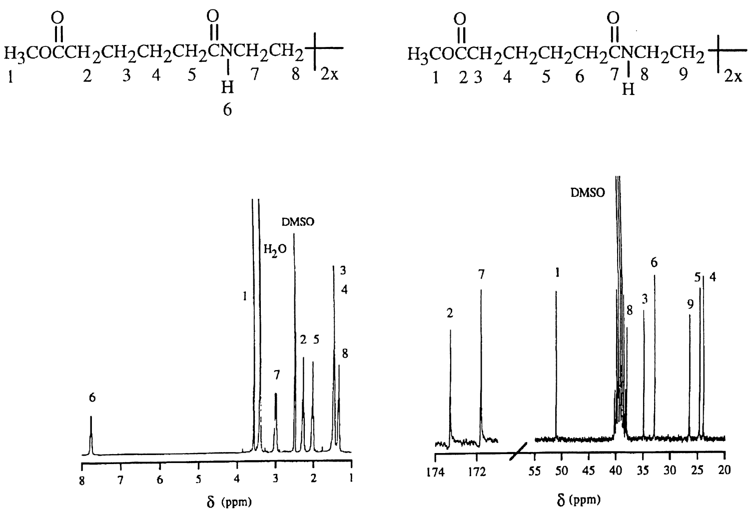
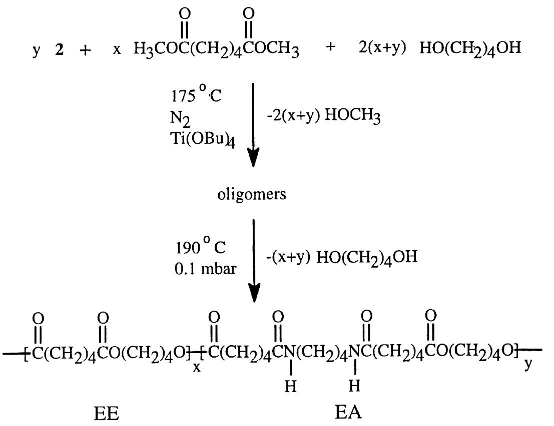


Fig. 1: ^{1}H NMR and ^{13}C NMR of 2 (DMSO-d_6)

These results showed that the formation of a cyclic imide, a stable six membered ring, is favoured and inhibits polymerization. Attempts to suppress imide formation by lowering polymerization temperatures were unsuccessful.



Scheme 3: Polycondensation of monomer 2, dimethyl adipate and 1,4-butanediol

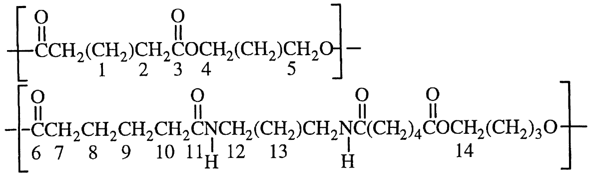
Succesful polymerization reactions were performed using monomer 2, dimethyl adipate and 1,4-butanediol in different feed compositions (Tab. 1). No cyclization reactions as described for monomer **1b** were observed. Polymers were obtained in almost quantitative yield and showed a high viscosity in the melt. Polymer compositions were calculated from the ^{1}H NMR spectra and were in good agreement with the expected polymer compositions based on feed ratios.

Tab. 1. Poly(ester-amide)s based on 2, dimethyladipate and 1,4-butanediol

polymer	feed composition[a)] (2)	dma	polymer composition[b)] [EE]x:[EA]y	yield
	mol%		mol/mol	wt %
2-100/0	0	33.3	100: 0	98
2-75/25	11.1	22.2	74:26	97
2-50/50	16.7	16.7	50:50	99
2-25/75	22.2	11.1	25:75	98
2-0/100	33.3	0		99
2-50/50-E[c)]	16.7	16.7	46:54	93

[a)] dma = dimethyl adipate; 1,4-butanediol: 66.7 mol %,
[b)] determined with 1H-NMR,
[c)] 1,2 ethanediol was used instead of 1,4-butanediol

A detailed structure analysis could be performed with ^{13}C NMR with special focus on the sequence distribution and the uniformity of the small amide blocks. Fig. 2 presents the ^{13}C NMR spectrum of polymer 2-50/50 in TFA-d1. Using the spectra of both homopolymers the carbon resonances could be distinguished and assigned. The ^{13}C NMR spectrum of the homopoly(ester-amide) 2-0/100 only revealed two signals in thecarbonyl carbon region, which showed that no ester-amide interchange had occurred during the polycondensation reaction. The signals 14 and 4 (as well as signals 11, 3 and 6) of the copolymers are found at different chemical shifts which shows that the esters which are the nearest to the amide sequence can be distinguished from esters that are linked to an adipate moiety. The differences in chemical shifts were not sufficiently large to distinguish between different triad sequences. Therefore a 50/50 copolymer with the shorter 1,2-ethanediol was synthesized as a model polymer in order to determine the triad distribution on the bases of differences in chemical shifts of the possible ester sequences.



$$\left[-\overset{O}{\overset{\|}{C}}CH_2(CH_2)CH_2\overset{O}{\overset{\|}{C}}OCH_2(CH_2)CH_2O-\right]-\left[-\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}\underset{H}{N}CH_2(CH_2)CH_2\underset{H}{N}\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{O}{\overset{\|}{C}}OCH_2(CH_2)_3O-\right]$$

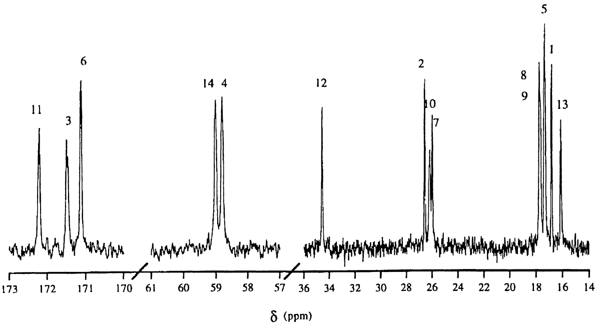


Fig. 2: ^{13}C NMR spectrum of polymer 2-50/50. solvent: TFA-d$_1$

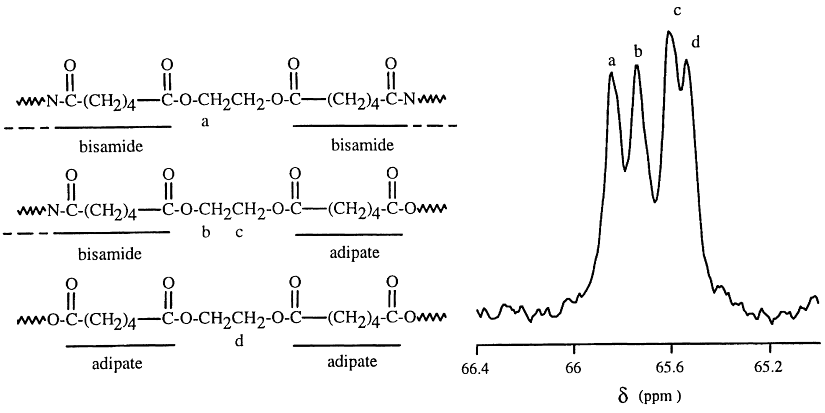


Fig. 3: left: triad sequences; right: expanded ^{13}C NMR spectra of $C(O)O\text{-}\underline{C}H_2$- region of polymer 2-50/50E

The sequence distribution of the amide blocks can be determined from ^{13}C NMR if the different triads can be distinguished. The three different triads present in the polymers (Fig. 3) give rise to 4 different carbon atoms (a-d). Fig. 3 presents the expanded ^{13}C NMR spectrum of the ester region for polymer 2-50/50E. The four resonances corresponding to the three different triads are clearly visible. The sequence distribution can be calculated according to a method previously published[8)] and is expressed in a factor R. R=0 for a blend or diblock copolymer, 1 for a random copolymer and 2 for an alternating copolymer. Using a Lorentzian deconvolution method for the four partly overlapping signals, R was calculated to be 1.08, which indicates that a near random copolymer is formed.

Molecular weights of polymers based on monomer **2** were measured by GPC in chloroform using the universal calibration method (Tab. 2). Polymers with a high amide content were insoluble in chloroform and only an indication of the M_n's could be obtained by end group analysis using ^1H NMR because of the low intensity of -C<u>H</u>$_2$OH endgroup protons at δ=3.55. This indicates that molecular weights are higher than 10 000 g·mol^{-1}. Mn's were between 16 000 and 40 000 g·mol^{-1} which is in the range of commercially used polyamides. The molecular weight distribution M_w/M_n was always close to 2 which is the theoretically expected value for polycondensates.

Tab. 2. GPC results of polymers based on monomer 2

polymer	M_w [a)] g·mol^{-1} (GPC)	M_n [a)] g·mol^{-1}(GPC)	M_w/M_n [a)]	Intr. visc. [b)] 30°C (cm^3/g)
2-100/0	27 100	16 500	1.6	64
2-75/25	41 900	22 000	1.9	49
2-50/50	58 300	37 300	1.6	28
2-25/75		>10 000[c)]		
2-0/100		>10 000[c)]		
2-50/50-E	29 600	16 200	1.8	13

[a)] determined with the universal calibration method, solvent: $CHCl_3$,
[b)] solvent: $CHCl_3$, [c)] determined via endgroup analysis with ^1H NMR in TFA-d_1.

Conclusions

Uniform and symmetrical bisester-bisamide monomers were successfully prepared both by ring-opening of glutaric anhydride followed by esterification and by aminolysis of dimethyl adipate. Copolymerization of the glutaric amide monomer, dimethyl adipate and 1,4-butanediol was unsuccessful because of the formation of six-membered cyclic imide-endgroups.

Copolymerization of the adipate amide monomer, dimethyl adipate and 1,4-butanediol resulted in high molecular weight poly(ester-amide)s with small and uniform bisamide blocks. The uniform amide blocks are randomly distributed in the polymer chain.

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