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Synthesis and Characterization of Multiblock Poly(Ester-Amide-Urethane)s

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ABSTRACT

In this study, a multiblock copolymer containing oligo(3-methyl-morpholine-2,5-dione) (oMMD) and oligo(3-*sec*-butyl-morpholine-2,5-dione) (oBMD) building blocks obtained by ring-opening polymerization (ROP) of the corresponding monomers, was synthesized in a polyaddition reaction using an aliphatic diisocyanate. The multiblock copolymer (pBMD-MMD) provided a molecular weight of 40,000 $g \cdot mol^{-1}$, determined by gel permeation chromatography (GPC). Incorporation of both oligodepsipeptide segments in multiblock copolymers was confirmed by ^1H NMR and Matrix Assisted Laser Desorption/Ionization Time Of Flight Mass Spectroscopy (MALDI-TOF MS) analysis. pBMD-MMD showed two separated glass transition temperatures (61 °C and 74 °C) indicating a microphase separation. Furthermore, a broad glass transition was observed by DMTA, which can be attributed to strong physical interaction i.e. by H-bonds formed between amide, ester, and urethane groups of the investigated copolymers. The obtained multiblock copolymer is supposed to own the capability to exhibit strong physical interactions.

INTRODUCTION

Polydepsipeptides (PDPs) are alternating copolymers composed of α-amino acid and α-hydroxy acid repeating units [1]. The physico-chemical properties of PDPs can be tuned by the amino acid moieties. Oligo- and polydepsipeptides provide the capability to exhibit strong physical interactions by H-bonds formed between the ester and amide linkages of the individual polymer chains [2]. Synthesis of PDPs is typically performed by ring-opening polymerization (ROP) of the relevant morpholine-2,5-diones (MDs) [3, 4]. However, the molecular weight of PDPs obtained from ROP in bulk is limited by the precipitation of the polymer during polymerization. These low molecular weight oligodepsipeptides thus do not provide sufficient elasticity to enable e.g. processing from the melt. An alternative to gain high molecular weights, which can not be obtained by the bulk ring-opening polymerization of the monomers, is the linkage of low molecular weight building blocks in a polyaddition reaction in solution. In addition, different functions from the different building blocks can be integrated into the material.

However, multiblock copolymers with oligodepsipeptide segments have been only described as multiblock copolymers in combination with poly(ether ester) blocks [5, 6].

Therefore it should be interesting to explore multiblock copolymers solely consisting of the oligodepsipeptide building blocks.

In this article, multiblock copolymers comprising different oligodepsipeptides (oDPs) segments were synthesized by a polyaddition reaction using an aliphatic diisocyanate. The molecular weight of the obtained multiblock copolymer was characterized by ^{1}H NMR and GPC. Thermal and thermomechanical properties of the copolymer were studied by DSC and DMTA. Special emphasis was put on the investigation of a successful linkage of the building blocks by MALDI-TOF.

EXPERIMENTAL DETAILS

Materials

If not mentioned otherwise, catalyst and solvents were obtained from Sigma Aldrich (Seelze, Germany) and used as received. A mixture of isomeric 2,2,4- and 2,4,4-trimethylhexane diisocyanate (TMDI) was purchased from Aldrich. *L*-alanine and *L*-isoleucine were obtained from Roth (Karlsruhe, Germany). Tin(II) 2-ethylhexanoate (Sn(Oct)$_2$) was distilled three times before usage. Solvents were dried according to standard methods and distilled prior to usage. The monomer, 3-*sec*-butyl-morpholine-2,5-dione (BMD) was synthesized in a two-step procedure as described in ref.[7]. The synthesis of (3*S*)-methylmorpholine-2,5-dione (MMD) was performed according to the synthesis route described in reference [5]. Two different oDPs, oligoMMD (oMMD) and oligoBMD (oBMD) with number average molecular weights around 5000 g·mol^{-1} (Table I), were synthesized by ROP of the corresponding monomers catalyzed by Sn(Oct)$_2$.

Synthesis of multiblock copolymers

6.87 g (0.94 mmol) of oligoMMD (oMMD), 7.25 g (1.25 mmol) of oligoBMD (oBMD), 0.51 mL (2.59 mmol) of TMDI, 14.63 mg of dibutyltin dilaurate (ca. 0.1 wt%) and 25.9 mL of N-Methyl-2-pyrrolidone (NMP) were weighed and placed into a schlenk tube using a continuous flow of dry N$_2$. Afterwards, the reactor was immersed in a thermostated oil bath at 80 °C. The polymerization was monitored by IR analysis of the absorption band of the isocyanate in the IR spectrum at 2270 cm^{-1}. The polymerization reaction was completed when the bands assigned to isocyanate groups disappeared. Then the crude mixture was dissolved in 21 mL NMP, precipitated in a ten-fold excess of diethyl ether, and then dried in a vacuum oven until constant weight was achieved.

Film preparation

Films for tensile tests and dynamic mechanical thermal analysis (DMTA) were prepared by thermal pressing at 150 °C and 90 bar, using a Collin P200E laboratory polymer press. Afterwards, the films were tempered at 110 °C for 10 min and then slowly cooled to room temperature.

Characterization Methods

NMR spectra were recorded in solution in DMSO-d_6 with a Bruker DCX-500 spectrometer at room temperature. The protonated species of the related solvent in deuterated solvent was used as an internal standard. GPC measurements were performed with a GPC system consisting of a GRAM gel column (250 × 4.6 mm^2, Polymer Standard Service, Mainz, Germany), a gradient pump PU 980, an automatic injector AS 851, a multi wavelength detector MD-910, a RI-930 detector (all Jasco, Tokyo, Japan), and a viscosimeter η-1001 detector (WGE, Dr. Bures, Dallgow, Germany). Dimethylformamide (DMF) was used as an eluent with a flow rate of 0.25 $mL·min^{-1}$ at 35 °C. The universal calibrated molecular weight of the polymer sample (M_u) was obtained according to the Mark-Houwink equation by using the software Borwin-PDA ver 1.5 (Jasco, Tokyo, Japan) and WINGPC 6.2 (Polymer Standard Service, Mainz, Germany). DSC experiments were conducted on a Netzsch DSC 204 Phoenix (Selb, Germany) at heating and cooling rates of 10 $K·min^{-1}$ ranging between -20 °C and 200 °C in sealed aluminum pans. Blends of oBMD and oMMD were prepared by solution casting from chloroform solution in mass ratios of oBMD:oMMD of 2:1; 1:1; and 1:2. Dynamic Mechanical Thermal Analysis (DMTA) was carried out on an Eplexor 25 N (Gabo) equipped with a 25 N load cell using standard sample size (ISO 527-2/1BB). The static load was 0.80%, the dynamic load 0.4%, and the frequency 10 Hz. Matrix Assisted Laser Desorption/Ionization Time Of Flight Mass Spectroscopy (MALDI-TOF MS) was performed on a Biflex III spectrometer (Bruker Daltonik, Leipzig, Germany). Samples in amounts of 0.5 mg were dissolved in 1 mL tetrahydrofuran (THF). The solution of a mixture of *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) and sodium trifluoroacetate (NaTFA) in THF was used as matrix. Mechanical properties of the pBMD-MMD were investigated by tensile tests at 20 °C and 65 °C by a Zwick Z1.0 tensile tester (Zwick, Ulm, Germany) equipped with a temperature controlled thermo chamber (Eurotherm Regler, Limburg, Germany). Specimens with a thickness between 0.22 and 0.41 mm, a width of 2 mm, and a length of 20 mm were used for these tests. The stretching rate was kept constant at 5 $mm·min^{-1}$ for all tensile tests. Three to five samples were investigated.

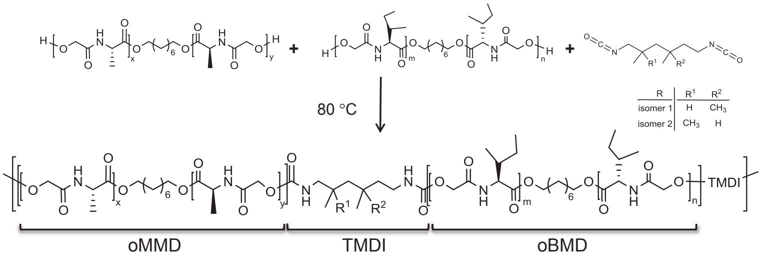
DISCUSSION

The oDPs were synthesized via ROP of the corresponding monomers. The molecular weight and thermal properties were determined by GPC and DSC analysis (Table I). Afterwards, the copolymerization reactions were performed according to Scheme 1.

Table I: Molecular weight and thermal properties of oDPs.

Sample ID	$M_{n,GPC}$[a] [$kg·mol^{-1}$]	M_w/M_n	T_g[b] [°C]	T_m[c] [°C]
oBMD	5.8 ± 0.2	1.2	65 ± 2	100 ± 1
oMMD	5.0 ± 0.2	1.1	59 ± 2	124 ± 2

[a] Number average molecular weight obtained from gel permeation chromatography (GPC).
[b] Glass transition temperature (T_g) determined by DSC measurements.
[c] Melting transition temperature (T_m) determined by DSC measurements.



Scheme 1. Synthesis of multiblock copolymer via TMDI as coupling reagent.

The composition of the multiblock copolymers was analyzed by ^{1}H NMR by determining the relevant proton signals of the specific MDs (Figure 1). The doublets between 1.28 and 1.38 ppm were assigned to the methyl groups in MMD units. The multiplets between 1.75 and 1.88 ppm as well as between 1.53 and 1.70 were assigned to the methylene and methine group in BMD. The ^{1}H NMR spectra of the oDP precursors are shown in the inset of Figure 1. Methyl groups from MMD units, methylene/methine groups from BMD units can be observed in the spectrum of the multiblock copolymer, which is a hint for the incorporation of the corresponding segments.

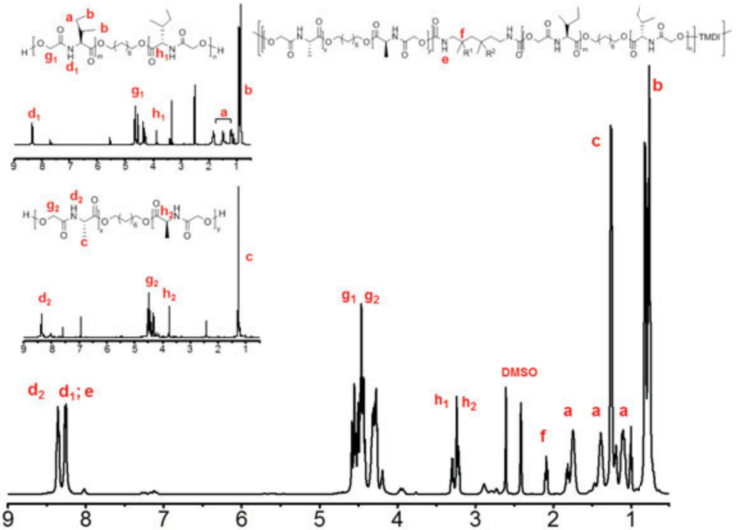


Figure 1. 500 MHz ^{1}H NMR spectrum of multiblock copolymer (pBMD-MMD) in DMSO-d_6.

In order to ascertain that TMDI is capable of linking both oBMD and oMMD segments, the obtained product was analyzed by MALDI-TOF MS. Figure 2 shows the MALDI-TOF MS spectrum of the reaction mixture obtained in the copolymerization reaction.

The mass ($M_{\text{pBMD-MMD}}$) of the copolymer composed of n_{oBMD} and n_{oMMD} building blocks can be expressed by equation 1:

$$M_{\text{pBMD}-\text{MMD}} = n_{\text{BMD}} M_{\text{BMD}} + n_{\text{MMD}} M_{\text{MMD}} + n_{\text{TMDI}} M_{\text{TMDI}} + (n_{\text{TMDI}} + 1) M_{\text{Initiator}} + M_{\text{Cat}} \quad (1)$$

where M_{BMD} and M_{MMD} are the mass of the BMD and MMD units. The n_{BMD}, n_{MMD} , and n_{TMDI} are the molar ratio of the BMD and MMD units as well as the linkage, respectively. (n_{TMDI}+1) correlates to the amount of initiator, since each segment contains at least one initiator unit. $M_{\text{initiator}}$ and M_{cat} represent the mass of the initiator unit and cation, which are 146 Da for 1,8-octanediol and 136 Da for NaTFA, respectively.

The MALDI-TOF spectrum of the resulting copolymer reveals the series corresponding to the random combinations of different precursor segments with verified chain length. The mass spacing corresponding to the mass of BMD and MMD units, i.e. 171 and 129 Da, respectively, indicates the coupling of the oBMD and oMMD segments. Coupling of the oBMD and oMMD segments with TMDI results in the formation of the copolymer pBMD-MMD. As shown in Table II, the masses of the resulting copolymers fit well with the calculated mass by equation (1). Coupling of oBMD and oMMD segments with TMDI occurred.

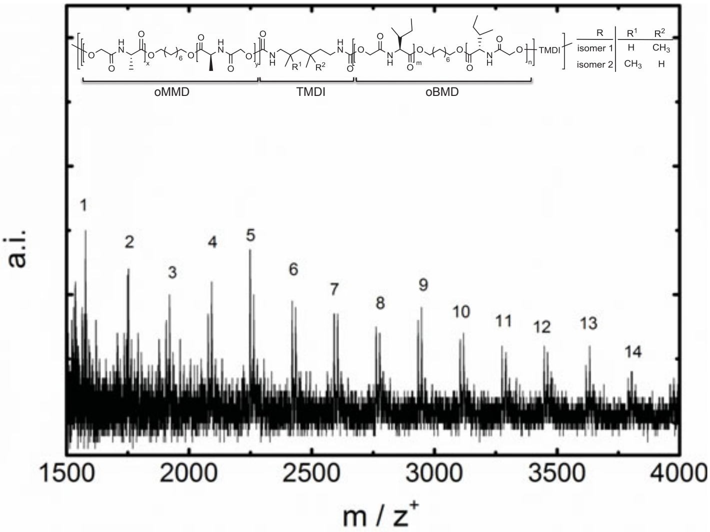


Figure 2. MALDI-TOF spectrum of pBMD-MMD.

Table II: Mass units of pBMD-MMD determined by MALDI-TOF MS analysis compared to calculated values. n_{MMD}: molar ratio of MMD units; n_{BMD}: molar ratio of BMD units; n(TMDI): molar ratio of linkage. M_{MMD} = 129 Da, M_{BMD} = 171 Da, M_{TMDI} = 210 Da, $M_{Initiator}$ = 146 Da, M_{Cat} = 136 Da.

Series	$\mathbf{n_{MMD}}$	$\mathbf{n_{BMD}}$	$\mathbf{n_{TMDI}}$	**m/z^+ Calculated**	**m/z^+ Found**
1	2	4	1	1580	1580
2	2	5	1	1751	1749
3	2	6	1	1922	1920
4	2	7	1	2093	2090
5	3	3	3	2250	2246
6	3	4	3	2421	2417
7	7	2	3	2595	2599
8	3	6	3	2763	2763
9	2	12	1	2948	2946
10	2	13	1	3119	3117
11	15	2	2	3271	3272
12	11	4	3	3453	3449
13	2	16	1	3632	3632
14	2	17	1	3803	3803

The observation of molecular weight increase studied by GPC also provided a secondary evidence for the linking of the different segments. As shown in Figure 3, the number average molecular weight (M_n) increased from 5,000 for oMMD to 40,000 g·mol^{-1} after copolymerization with oBMD. Thus the obtained multiblock copolymers consist of 8–9 oligomer building blocks in average.

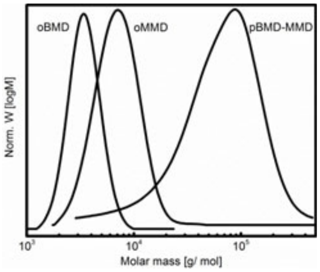


Figure. 3. Molecular weight distribution of oBMD, oMMD, and multiblock copolymer (pBMD-MMD) determined by means of GPC

Figure 4a displays the DSC thermogram corresponding to oBMD, oMMD and their blends of different compositions. Single T_gs are observed for blends with mass ratio of oBMD to oMMD ranging from 2:1 to 1:2. For all combinations, the values of T_g correlated well with those values estimated by the Flory-Fox equation. In this context, the observation of T_gs for the blend compositions can be considered as an indication for the miscibility of the low molecular weight building block originating from the structural similarity of the constituents

Compared to the single T_gs of the blends, the multiblock copolymer presented two well separated T_gs (61 °C and 74 °C) as shown in Figure 4b. The T_gs observed in the pBMD-MMD are both slightly higher than those of oBMD and oMMD, respectively. The increase of T_gs could be explained by the consumption of hydroxyl groups during polyaddition reactions, which results in a decrease of the free terminal groups. Meanwhile, the linkage of building blocks also led to a prolongation of polymer chains and in this way contributes to the phase segregation. Thus, the observation of well separated T_gs, which are higher than those of pure precursors, is a very strong hint for a microphase separation.

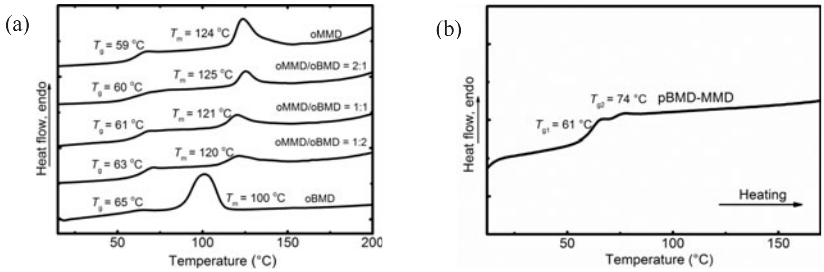


Figure 4. Thermal properties of (a) oBMD, oMMD and blends of oBMD / oMMD in mass ratios of 2:1; 1:1; 1:2; (b) pBMD-MMD.

The DMTA results showed a broad glass transition for pBMD-MMD (Figure 5), which was more than 40 °C. This may be attributed to the strong intermolecular hydrogen bonds formed between amide, ester, and urethane groups of the investigated copolymers.

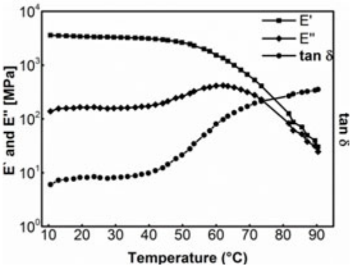


Figure 5. Thermomechanical properties of pBMD-MMD. E´: Storage Modulus, E´´: Loss Modulus, δ: Phase Angle.

The analytic data and mechanical properties of the multiblock copolymer are listed in Table III. At 20 °C, below the T_gs of both oligodepsipeptide segments, the multiblock copolymer was in the glassy state. pBMD-MMD showed characteristic mechanical properties of a hard material at this temperature, i.e., high Young`s modulus (*E*) with a value of 1555 MPa and low elongation at break (ε_b) with a value of 3%. At 65 °C, oMMD domains were in viscoelastic state, while the chain movement of oBMD segments was still restricted. At this temperature, *E* decreased significantly to a value of 0.5 MPa and ε_b increased to 700%.

Considering the results from tensile tests of multiblock copolymer pBMD-PPDO consisting of oligoBMD and oligo(p-dioxanone) (PPDO) segments [8], *E* obtained at 25 °C with a value of around 670 MPa, is around 3 times lower than that of pBMD-MMD at 20 °C. The difference can be attributed to the much stronger physical interactions between amide and ester bonds of pBMD-MMD compared to pBMD-PPDO. When the measurements were performed at 65 °C, pBMD-MMD displayed a significant difference in elongation at break, which was eleven times higher than pBMD-PPDO measured at 75 °C. This much higher ε_b of pBMD-MMD can be attributed to the higher stability due to the existence of strong physical interaction.

Table III: Mechanical properties of pBMD-MMD and pBMD-PPDO. T_{test}: the temperature when test was performed. *E*: Young`s modulus, ε_b: elongation at break.

Sample ID	T_{test} **[°C]**	T_g **[°C]**	T_m **[°C]**	*E* **[MPa]**	ε_b **[%]**
pBMD-MMD	20	61; 74	n.d.[a]	1555 ± 186	3 ± 0.5
	65			0.5 ± 0.2	700 ± 30
pBMD-PPDO	25	-8; 40	60; 82	670 ± 34	13 ± 0.3
	75			33 ± 5.0	60 ± 10

[a] n.d.: not detectable.

CONCLUSIONS

In summary, the obtained results demonstrate successful synthesis of novel depsipeptide-based multiblock copolymers (pBMD-MMD) with a molecular weight of 40,000 $g \cdot mol^{-1}$. The incorporation of different segments was confirmed by ^1H NMR, MALDI-TOF MS as well as GPC. Compared to the blends of oBMD and oMMD for which only one T_g was determined for each blend composition, the two T_gs observed in the DSC thermogram of pBMD-MMD indicated a phase segregation of the oligodepsipeptide building blocks. This can be considered as a second evidence in addition to the results from MALDI-TOF for the integration of both oBMD and oMMD blocks. The broad T_g obtained from DMTA measurement indicated the existence of strong physical interactions. It has been shown that by varying the amino acid moieties, the physico-chemical properties of the obtained multiblock copolymer can be adjusted. In this way, the multiblock copolymer pBMD-MMD may be promising candidate material, where slow degradation and a T_g around body temperature could be beneficial.

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