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Materials and methods

Materials. All solvents were dried and distilled using standard procedures [1]. N,N-dimethylformamide (DMF) was dried using standard procedures, degassed by freeze-pump-thaw procedure and stored under nitrogen atmosphere at -30°C. Diethyl ether and tetrahydrofuran were dried using standard procedures and degassed by freeze-pump-thaw procedure. Methylmethacrylate (90% Acros) was destilled from CaH_2 under reduced pressure and was stored under nitrogen atmosphere at -30°C. Cu(I)Br (98% Fluka) was purified according to the published procedure [1]. Triethylamine (p.a. Acros) was dried over CaH_2, destilled and stored under nitrogen. γ-benzyl-L-glutamic acid (>99%, Fluka), phosgene solution (20% in toluene, Fluka), 2,2'-bipyridine (bpy) (99% Acros), hexamethyltriethyltetraamine (HMTETA, 97%, Aldrich), dimethylsulfoxid (DMSO, Acros) were used as received. γ-benzyl-L-glutamic acid-*N*-carboxyanhydride (BLG-NCA) was synthesized according to the literature [2].

Double headed Initiator. The synthesis of **alloc-L-leucine-*N*-hydroxysuccinimidyl ester (1)** and its use for preparation of alloc amides is described in [3, 4]. **Alloc-L-leucin-α-bromo-isobutyric acid 2-aminoethanol ester (4)** was synthesized from alloc-L-leucine-*N*-hydroxysuccinimidyl ester with aminoethanol and α-bromo-isobutyric acid bromide in a two-step reaction. 5.30 g (16.97 mmol) Alloc-L-leucine-*N*-hydroxysuccinimidyl (1) ester was dissolved in 30 mL THF and 1.5 mL (25.45 mmol) aminoethanol was added. The mixture was stirred for 1 h at room temperature. The white precipitate was filtered off and the filtrate was concentrated. The crude product was dissolved in ethyl acetate, washed with dilute aqueous HCl (2 × 50 mL), with saturated aqueous $NaHCO_3$ (2 × 50 mL), with saturated aqueous NaCl

(2 × 50 mL) and subsequently dried over sodium sulfate. The solvent was then evaporated in vacuo to leave the product (3.5 g, 13.6 mmol, 80%).

^{1}H NMR ($CDCl_3$, ppm): 0.94 (dt, 6H, ^{3}J= 4.6, ^{4}J=1.5 Hz , $(C\underline{H}_3)_2$-CH-);1.54, 1.65 (2*m, 1+1H), $((CH_3)_2$-CH-$C\underline{H}_2$-); 2.00 (m, 1H, $(CH_3)_2$-$C\underline{H}$-CH_2-); 3.22 (s, 1H, $\underline{H}O$-CH_2-); 3.42 (m, 2H, -$C\underline{H}_2$-NH-); 3.70 (m, 2H, HO-$C\underline{H}_2$-CH_2-); 4.18 (dd, 1H, ^{3}J= 8.6, -NH-C$\underline{H}$-); 4.56 (s, 2H, (-$C\underline{H}_2$-O-); 5.22 (dd, 1H, ^{2}J=1.2 Hz, ^{3}J= 10.4 Hz, ($C\underline{H}_2$=CH-); 5.30 (dd, 1H, ^{2}J=1.5 Hz, ^{3}J= 17.2 Hz, ($C\underline{H}_2$=CH-); 5.90 (m, 1H, (CH_2=C$\underline{H}$-CH_2-); 6.87 (s , 1H,);9,23 (d, 1H,)

^{13}C NMR ($CDCl_3$, ppm): 21.9 (($\underline{C}H_3)_2$CH-), 22.9 (($\underline{C}H_3)_2$CH-), 24.7 (($CH_3)_2\underline{C}$H-CH_2-), 41.5 (($CH_3)_2$CH-$\underline{C}H_2$-), 42.3 ($CH_2\underline{C}H_2$NH-), 53.7 (($CH_3)_2$CH-CH_2-$\underline{C}$H-), 66.0 (OH-$\underline{C}H_2$-CH_2-), 67.7 (CH_2=CH-$\underline{C}H_2$-O-), 117.9 ($\underline{C}H_2$=CH-), 132.4 (CH_2=$\underline{C}$H-CH_2), 156.4 (-O-$\underline{C}$(O)-NH-), 173.4 (-CH-$\underline{C}$(O)-NH-)

1.68 g (6.5 mmol) Alloc-L-leucine-aminoethanol (2) was dissolved in 10 mL THF and 1.2 mL (8.9 mmol) triethylamine (abs.) was added. After cooling to 0°C, 1.1 mL (8.90 mmol) α-bromoisobutyric acid bromide (3) (dissolved in 5 mL THF) was added in small amounts. A white precipitate of triethylammonium bromide was observed. The mixture was allowed to react over night at room temperature. The precipitate was filtered off and the filtrate was concentrated. The crude product was dissolved in chloroform, washed two times with saturated aqueous $NaHCO_3$, with water and then with saturated aqueous NaCl followed by drying over sodium sulfate. Flash chromatography (chloroform:diethyl ether 1:1) gave 2.00 g of product (4.91 mmol). Yield: 75 %.

^{1}H NMR ($CDCl_3$, ppm): 0.94 (dd, 6H, ^{3}J= 6.0 Hz, ^{4}J=2.1 Hz, $(C\underline{H}_3)_2$-CH-); 1.51 (m, 1H, $(CH_3)_2$-$C\underline{H}$-CH_2-); 1.67 (m, 2H), $(CH_3)_2$-CH-$C\underline{H}_2$-); 1.94 (s, 6H, Br$(C\underline{H}_3)_2$-C-); 3.59 (m, 2H, -CH_2-$C\underline{H}_2$-NH-); 4.15 (m, 1H, -HN-C$\underline{H}$-), 4.27 (t, 2H, ^{3}J= 5.3 Hz, -O-$C\underline{H}_2$-CH_2-); 4.57 (d, 2H,

^{3}J= 5.5 Hz, (CH_2=CH-C$\underline{H}_2$-O-); 5.19, (m, 1H, (C$\underline{H}_2$=CH-); 5.25 (m, 1H, (C$\underline{H}_2$=CH-); 5.91 (m, 1H, (CH_2=C$\underline{H}$-CH_2-O-); 6.48 (s, 1H, -N$\underline{H}$-);

^{13}C NMR ($CDCl_3$, ppm): 21.9 (($\underline{C}H_3)_2$CH-), 23.0 (($\underline{C}H_3)_2$CH-), 24.7 (($CH_3)_2\underline{C}$H-CH_2-), 41.5 (($CH_3)_2$CH-$\underline{C}H_2$-), 30.6 (Br($\underline{C}H_3)_2$-C-), 38.4 (-$CH_2\underline{C}H_2$NH-), 41.3 (($CH_3)_2$CH-$\underline{C}H_2$-), 53.5 (($CH_3)_2$CH-CH_2-$\underline{C}$H-), 59.5 (($CH_3)_2$Br-$\underline{C}$-C(=O)O-), 64.3 (-O-$\underline{C}H_2$-CH_2-), 66.0 (CH_2=CH-$\underline{C}H_2$-O-), 118.0 ($\underline{C}H_2$=CH-), 132.4 (CH_2=$\underline{C}$H-CH_2-), 156.4 (-O-$\underline{C}$(O)-NH-), 171.5 (-C-$\underline{C}$(=O)-O-), 172.5 (-CH-$\underline{C}$(O)-NH-)

IR (KBr pellet, in cm^{-1}): 3310 (N-H, valence), 2957 (aliphatic C-H), 1736 (C=O), 1663 cm^{-1} (amide I), 1532 cm^{-1} (amide II)

The initiator **(phen)Ni(amido Amdate) complex (5)** was synthesized following a procedure similar to the method published by DEMING [4]. 328 mg (1.82 mmol) 1,10 phenanthroline (phen) (dissolved in 15 mL DMF (abs.)) was added under a nitrogen atmosphere to 500 mg (1.82 mmol) Ni(COD)$_2$ suspended in 40 ml DMF (abs.). The mixture was stirred at room temperature for two hours to form a (phen)Ni(COD) solution and subsequently 740 mg (1,82 mmol) Alloc-L-leucin-α-bromo-isobutyric acid 2-aminoethyl ester (4) (dissolved in 10 mL DMF (abs.)) was added. The mixture was allowed to react over night at room temperature and then heated up to 50°C for 24 hours. The product was isolated from this green solution by precipitation into 170 mL diethyl ether (abs.). After washing with THF (2 × 100ml) and drying in vacuo a green powder was obtained (0.50 g (0.89 mmol), 49% yield).

IR (KBr pellet, in cm^{-1}): 3385 (N-H, valence), 3051 (C-H-valence, aromatic), 2961 (C-H, valence aliphatic), 1717 (C=O, ester), 1654 (amide I, C=O-valence), 1516 (amide II, C=O-valence)

Elemental analysis (calculated values in parenthesis): N 8.52% (10.00%); C: 44.90% (51.46%); H 3.86% (5.22%); Br 16.96% (14.27%), Rest (should be Ni): 25.76% (19.05%)

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Polymerization of **γ-benzyl-L-glutamate-*N*-carboxyanhydride** (macroinitiator). γ-BLG-NCA was dissolved in DMF (abs.) and transferred with a syringe to the initiator (dissolved in (DMF (abs.)) under nitrogen atmosphere. The mixture was stirred for 16 hours at room temperature. The polymer solution was precipitated into cool methanol (0°C) with a small concentration of HCl (4 mM HCl) to destroy the nickel complex. The polymer was isolated and reprecipitated two times from THF into methanol.

^{1}H-NMR ($CDCl_3$, ppm): 2.19 (s, 2H, -C$\underline{H}_2$-CH_2-CO-O-CH_2-C_6H_5), 2.48 (s, 2H, -CH_2-C$\underline{H}_2$-CO-O-CH_2-C_6H_5), 3.85 (s, 1H, -NH-CO-C$\underline{H}$(R)-), 4.93 (s, 2H, C_6H_5-C$\underline{H}_2$-O-CO-), 7.14 (s, 5H, $C_6\underline{H}_5$-CH_2-O-CO-), 8.47 (s, 1H, N$\underline{H}$)

^{13}C-NMR ($CDCl_3$, ppm): 25.5 (-$\underline{C}H_2$-$\underline{C}H_2$-CO-O-), 30.8 (-NH-CO-$\underline{C}$H(R)-), 66.5(-CO-O-$\underline{C}H_2$-C_6H_5), 128.1 (benzyl group), 128.5 (benzyl group), 135.7 (substituted C, aromatic), 172.6 (-CH_2-CH_2-$\underline{C}$O-O-CH_2-C_6H_5), 175.5 (-NH-$\underline{C}$O-CH(R)-)

IR (KBr pellet, in cm^{-1}): 3290 (N-H-valence), 3035 (C-H-valence, aromatic), 2955 (C-H-valence, aliphatic), 1734 (C=O-valence, ester), 1653 (amide I, C=O-valence), 1549 (amide II, C=O-valence), 1454 (C-H-deformation, aliphatic)

Block copolymerization. A dry round bottomed flask was charged with Cu(I)Br and macroinitiator dissolved in DMF (abs.), the solution was degassed by bubbling with nitrogen for 15 minutes. The ligand (HMTETA or bipy), MMA and anisole as internal standard were added. The polymerisation was done at 80 °C and 90°C, respectivly. After the desired polymerization time the catalyst was removed by an alox column and the polymer was precipitated into methanol, isolated and reprecipitated two times.

^{1}H-NMR ($CDCl_3$; 400 MHz, δ in ppm): 0.78, 0.95, 1.18 (3* s, 3H, α-C$\underline{H}_3$-), 1.75 (s, 2H, -C$\underline{H}_2$- from PMMA-block) 2.01 (s, 2H, -C$\underline{H}_2$-CH_2-CO-O-), 2.33 (s, 2H, -CH_2-C$\underline{H}_2$-CO-O-),

3.54 (s, 3H, C<u>H</u>$_3$-O-CO-C-), 3.60 (s, 1H, -NH-CO-C<u>H</u>(R)-), 4.96 (s, 2H, C_6H_5-C<u>H</u>$_2$-O-), 7.18 (s, 5H, C_6<u>H</u>$_5$-CH_2-O-)

^{13}C-NMR ($CDCl_3$, 100 MHz, δ in ppm): 24.3 (CH_3-C-), 25.2 (-<u>C</u>H_2-<u>C</u>H_2-CO-O-), 30.5 (-NH-CO-<u>C</u>H(R)-), 51.7 (<u>C</u>H_3-O-CO-C-), 66.1(-CO-O-<u>C</u>H_2-C_6H_5), 127.7 (benzyl group), 128.2 (benzyl group), 135.5 (substituted C, aromatic), 172.6(-CH_2-<u>C</u>O-O-CH_2-C_6H_5)

IR (KBr pellet, in cm^{-1}): 3288 (N-H-valence), 3036 (C-H-valence, aromatic, 2959 (C-H-valence, aliphatic), 1734 (C=O-valence, ester), 1624 (amide I), 1521 (amide II), 1454 (C-H-deformation, aliphatic)

MALDI-TOF mass spectral analysis:

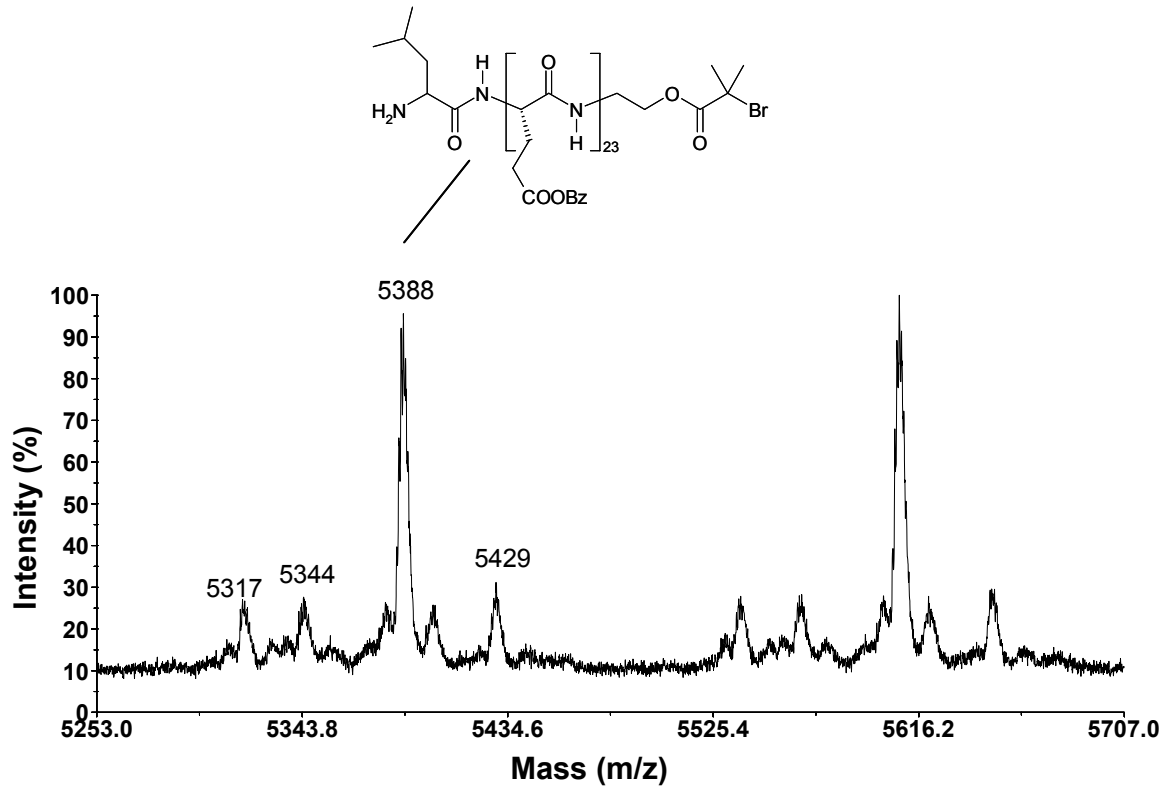

Figure 2: Detailed MALDI-TOF spectrum of PBLG initiated with 5. The mayor peak can be assigned to the proposed structure of the macroinitiator. The smaller peaks are not yet assigned, but are neither pure PBLG (without endgroups) nor PBLG with only one of the endgroups.

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Characterization. Polymer conversions were determined by investigation of monomer consumption by gas chromatography. Molecular weights and molecular weight distributions were measured by SEC/LS combination in DMF (membrane filtered and degassed) containing LiBr (0.1 mol%) on two PL-gel 5µm mixed-C columns (Polymer Laboratories) at 80°C and a flow rate of 0.5 mL/ min. Detection was performed with a Melz LCD201 differential refractive-index detector (set at 35°C), a Thermo Separation Products UV150 Spectraseries UV-visible light detector set at 270nm, and a TriStar MiniDawn light scattering detector from Wyatt Technology (angles at 30, 90, and 120°). ^{1}H NMR and ^{13}C NMR measurements were conducted on a Bruker AM400 FT-spectrometer (400MHz). Sample concentrations were 30-40 mg/mL for ^{1}H, and for ^{13}C spectra, respectively. Tetramethylsilane was used as internal standard. Mass spectra were recorded on Finnigan MAT112 and MAT SSQ7000 instruments at an ionization potential of 70eV.

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