Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting information for

Poly(3-ethylglycolide): A well-defined polyester matching the hydrophilic hydrophobic balance of PLA

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(*rac*)-3-Ethyl-1,4-dioxane-2,5-dione (EtGly):

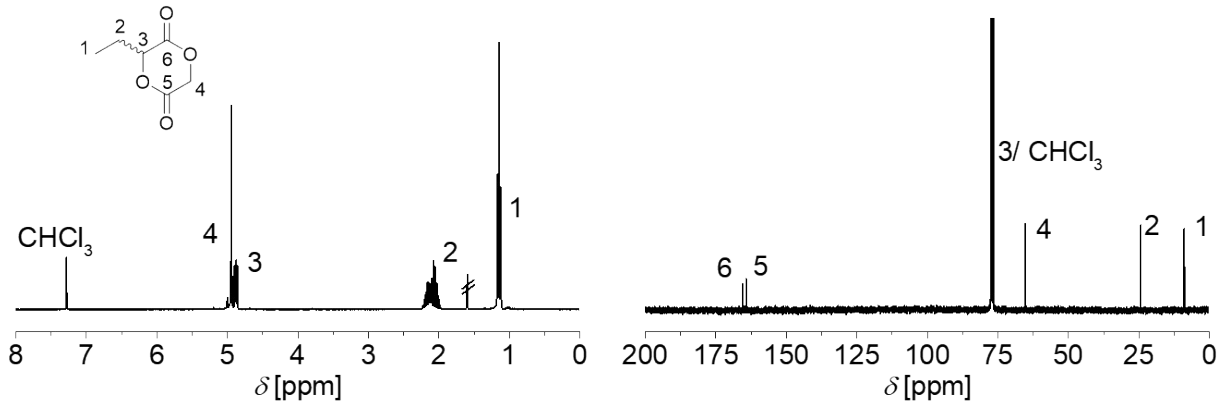


Figure S1: NMR characterization of the monomer EtGly (300 MHz, $CDCl_3$) and structural assignment of the signals. **Left**: ^{1}H-NMR spectrum. **Right**: ^{13}C-NMR spectrum.

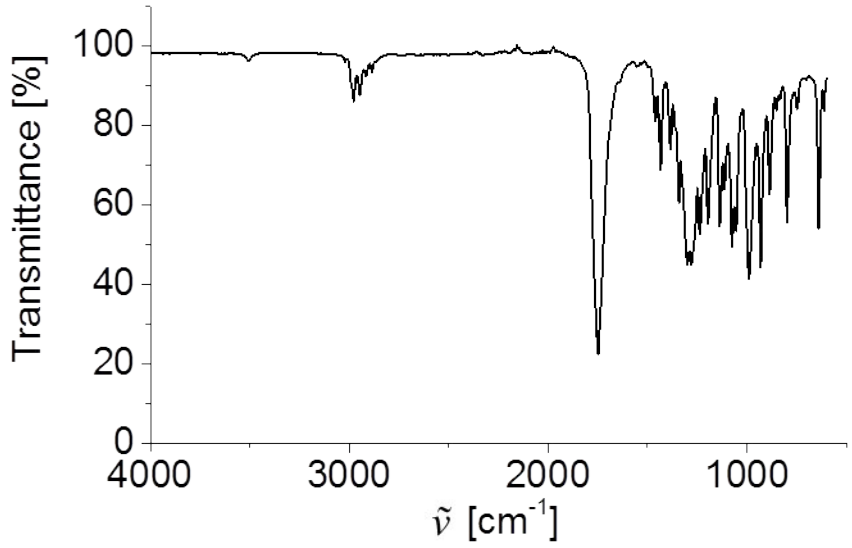


Figure S2: FT-ATR-IR transmittance spectrum of the monomer EtGly.

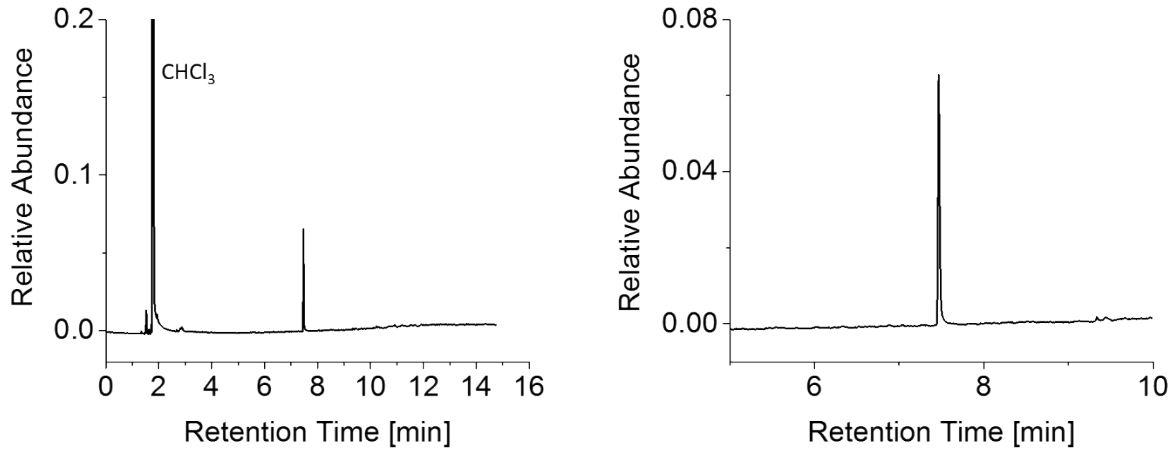


Figure S3: GC-FID chromatogram of the monomer EtGly (60 to 200 °C, heating rate 16 °C min^{-1}). **Left**: Full chromatogram. **Right**: Zoom into the region from 7 to 8 minutes.

Further discussion of the characterization of EtGly by means of mass spectrometry

Instrumentation

For GC-HRMS-measurements the following MS parameters were set: Resolution 120,000; AGC target 1×10^6; maximum ion time: 200 ms; scan range 50 to 600 *m/z*; transfer line 1, 2 were at 280 °C and transfer line 3 at 250 °C. The ion source temperature was 300 °C and a combined EI/CI ion volume was installed. The filament delay was 3.90 min and the acquisition was performed between 4 and 23 min. For the CI mode methane 5.5 (Air Liquide, Düsseldorf, Germany) at a flow rate of 2 mL× min^{-1} was used. The Thermo GC trace 1310 coupled to a TriPlus RSH auto sampler was used with the following parameters: After initial 2 minutes at 40 °C the GC oven temperature was raised to 325 °C with 15 °C × min^{-1} and held for 2 min at 325 °C. The PTV injector was operated in split mode at 250 °C with a flow rate of 16 mL × min^{-1}, split flow was 16 and the column flow 1 mL× min^{-1} in constant flow mode. The septum pure flow was set to 2 mL× min^{-1}. After initial one minute at 250 °C the injector was

raised to 350 °C for one minute with a flow rate of 50 mL× min^{-1} to clean the injector. The sample was injected using a 10 µL gas tight syringe after washing the syringe once with ethyl acetate and once with heptane. Before injection the syringe was rinsed thrice with 1 µL of the sample and three plunger strokes were applied to prevent air bubbles. Bottom sense was enabled and the sample was taken 0.2 mm above the bottom of the vial.

Results and discussion

Unfortunately, the expected mass of m/z = 144 was not detected by ESI MS (**Figure S4**). Instead, m/z = 455.12 and m/z = 471.10 were assigned to $[3M+Na]^+$ and $[3M+Na]^+$, respectively. These values could either result from physical adducts of three EtGly with a sodium or potassium ion, respectively, or from the isobaric macrocyclic trimer. Even if present only in trace amounts, the macrocyclic trimer could potentially be favorably ionized due to an easy complexation of the cation.[1] Aiming towards a distinction of the two possibilities, GC HRMS measurements were conducted utilizing both, EI as well as CI MS. **Figure S5** depicts the chromatograms of the total ion current (TIC). As confirmed by the EI and CI mass spectra, EtGly eluted at 9 min (group A, **Figure S6**). Additional peaks were detected at higher elution times, corresponding to column temperatures above 250 °C. Their intensity was significantly higher in GC-MS using EI compared to GC-MS performed with the milder CI method. The peaks were assigned to macrocycles composed of two or three EtGly, respectively. Similar species have been commonly detected by pyrolysis GC-MS of PLA,[2-5] where various GC fractions were assigned to diastereomers. As a) such high temperatures come close to experimental conditions for GC-MS pyrolysis of PLA,[2] and b) PEtGly was prone to thermal degradation at even lower temperatures (see below for TGA thermograms), it could not be excluded that the monomer EtGly was prone to reaction during the GC MS analysis, thereby producing the detected macrocycles.

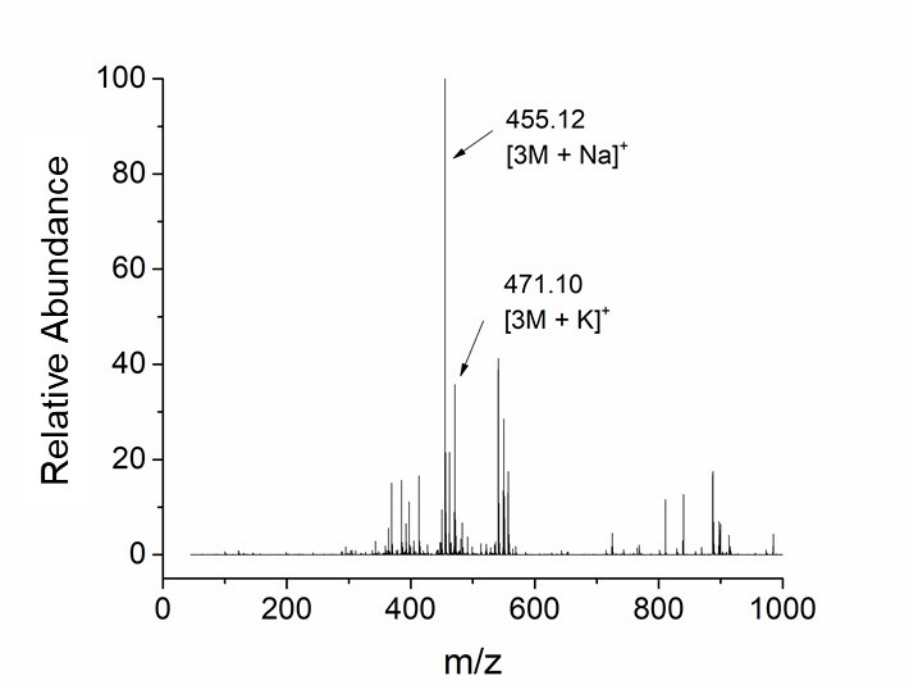


Figure S4: ESI mass spectrum (positive mode) of the monomer EtGly and structural assignments.

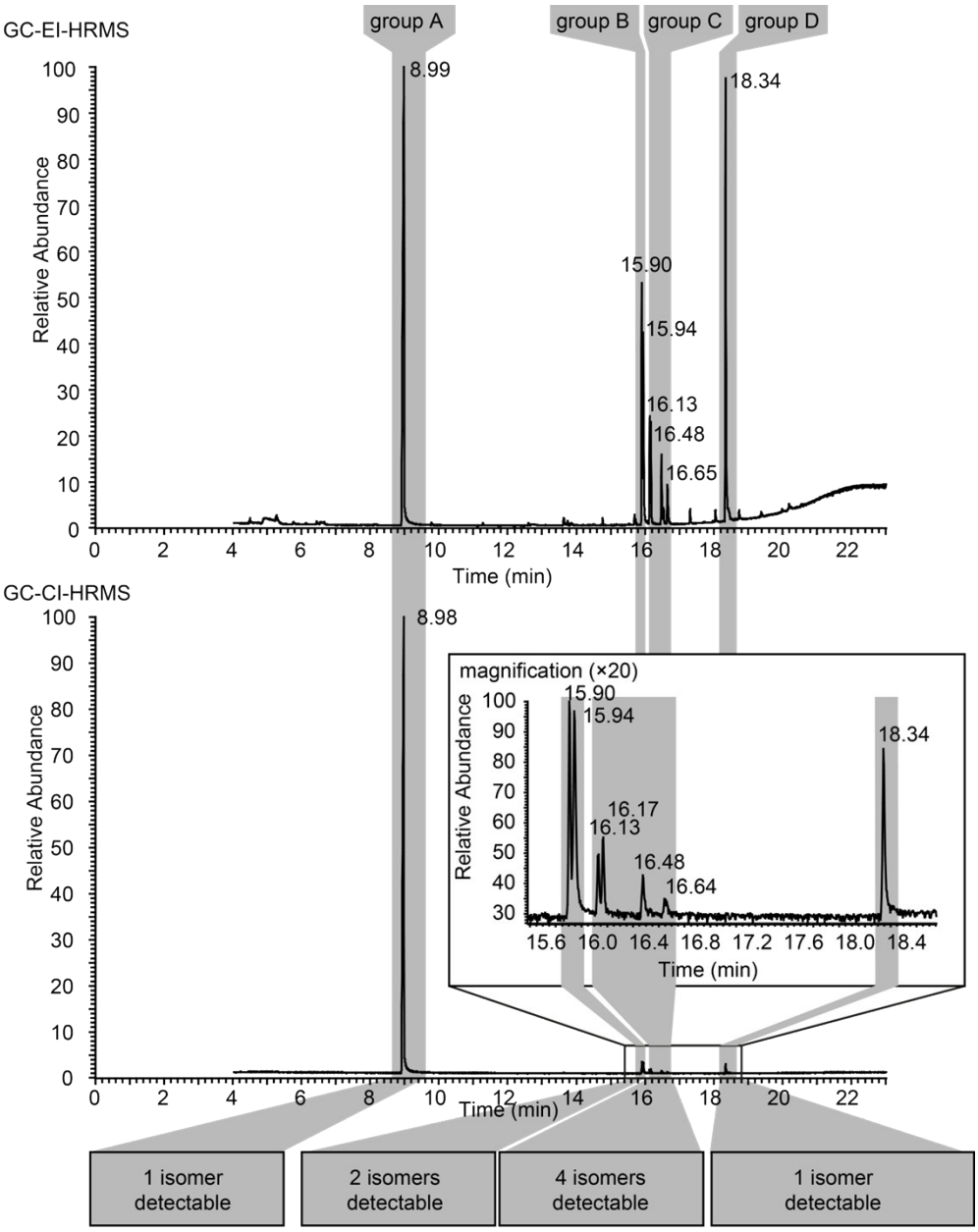
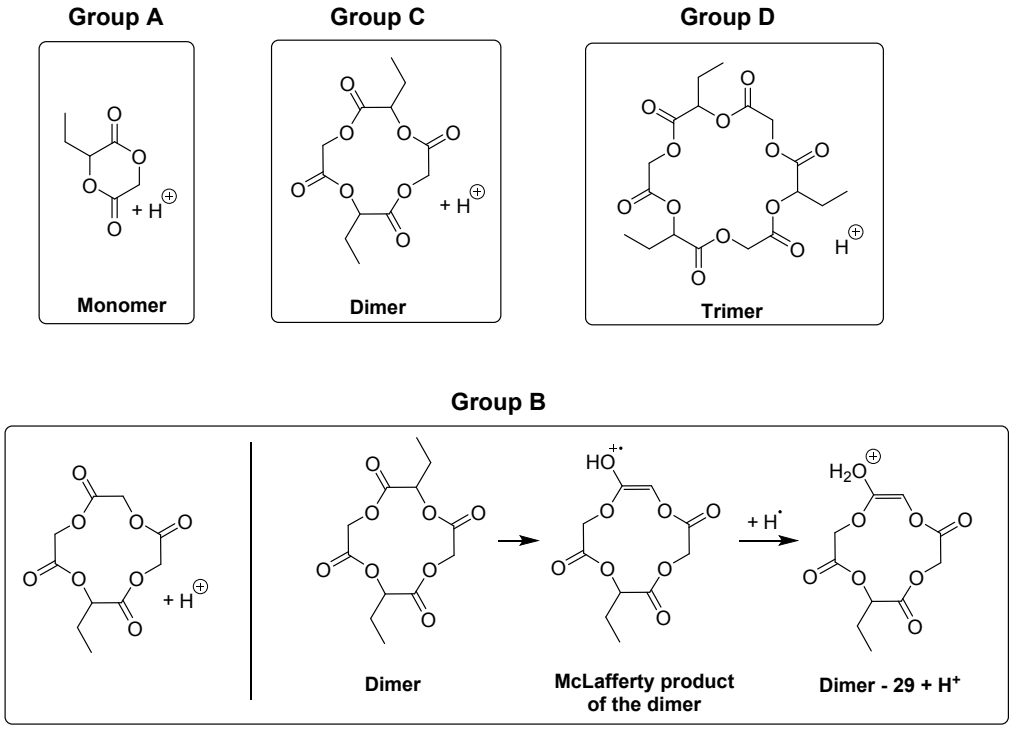


Figure S5: GC-chromatograms of the total ion current (TIC) of EtGly. **Top**: TIC from EI-ionization. **Bottom**: TIC from CI ionization including magnification. Based on their mass spectra, the peaks were assigned to four different compound groups (A to D, see **Table S1** and **Scheme S1**).

Table S1: Assignment of the peaks detected during GC-MS analysis of EtGly. TIC are depicted in Figure S5.

Peak number	**t_{el} [min]**	**Group**	**Assignment**	**m/z CI [M+H]$^+$**	**m/z EI**
1	8.99	A	monomer	145	116; 58
2	15.90	B	dimer – 29[a)]	261	244; 168; 128; 101
3	15.94	B	dimer – 29 [a)]	261	244; 168; 128; 101
4	16.13	C	dimer	289	272; 214; 186; 128; 70
5	16.17	C	dimer	289	272; 214; 186; 128; 70
6	16.48	C	dimer	289	272; 214; 186; 128; 70
7	16.64	C	dimer	289	272; 214; 186; 128; 70
8	18.34	D	trimer	433	272; 186; 128

[a)] Compare **Scheme S1**.



Scheme S1: Schematic representation of the structure of the different species assigned by GC-MS analysis. The structure assigned to group B signals can either represent the protonized

molecular ion depicted on the bottom left, or be formed by McLafferty rearrangement of the dimer followed by addition of a hydrogen radical during CI.

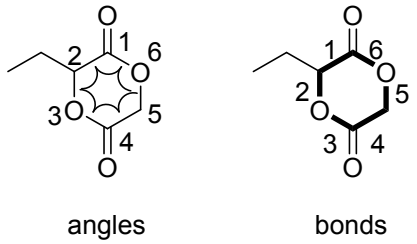


Figure S6: Schematic representation of the bond angles and lengths of the endocyclic atoms of EtGly used in **Table S1**.

Table S2: Bond angles and lengths of the endocyclic atoms of EtGly.

M1	**1**	**2**	**3**	**4**	**5**	**6**
Bond angle [°]	116.3	110.9	117.3	116.7	113.6	118.7
Bond length [Å]	1.51	1.46	1.34	1.50	1.44	1.34

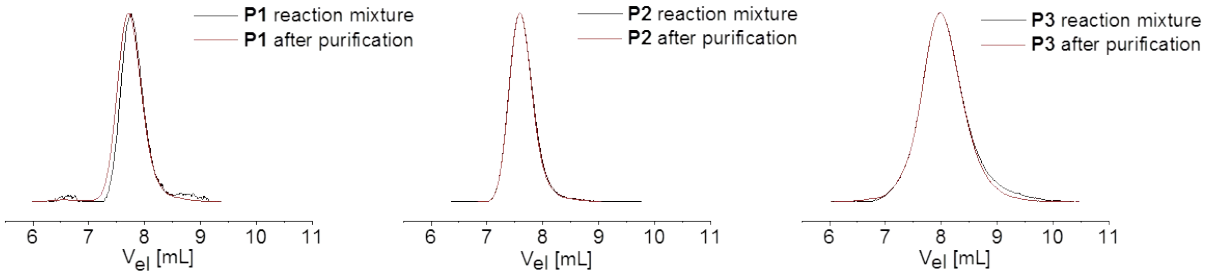


Figure S7: SEC elugrams ($CHCl_3$, RI detection) of the homopolymers from reaction mixture (black) and after purification (red). **Right**: PLLA (**P1**). **Center**: **P2** PDLA (**P2**). **Left**: PEtGly (**P3**).

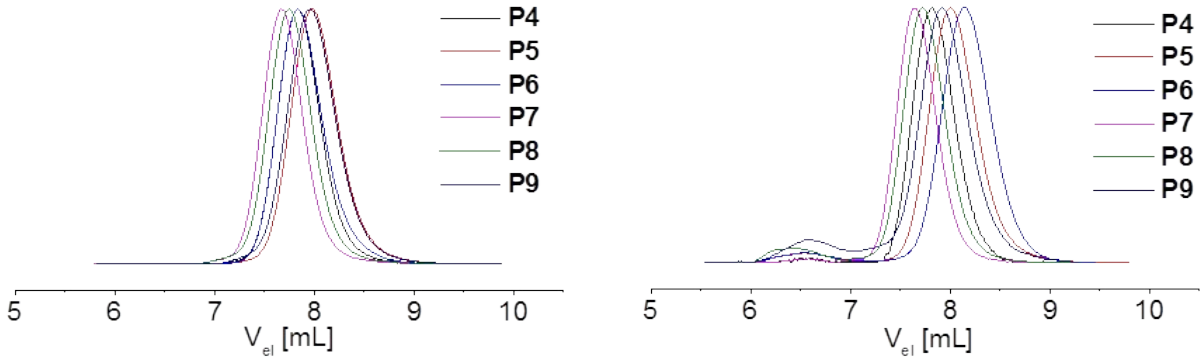


Figure S8: SEC elugrams ($CHCl_3$, RI detection) of the statistical copolymers **P4-P9**. **Left**: Elugrams after quenching of the polymerization solution. **Right**: Elugrams after precipitation.

Poly(L-lactide) (**P1**):

800 mg L-Lactide (5.55 mmol) were dissolved in 18.50 mL toluene and the ROP was initiated using 111 µL stock solution consisting of 5.74 µL BnOH (0.06 mmol), 7.97 µL mTBD (0.06 mmol) and 97.29 µL toluene. The polymerization was quenched by addition of 27.4 mg benzoic acid (0,22 mmol).

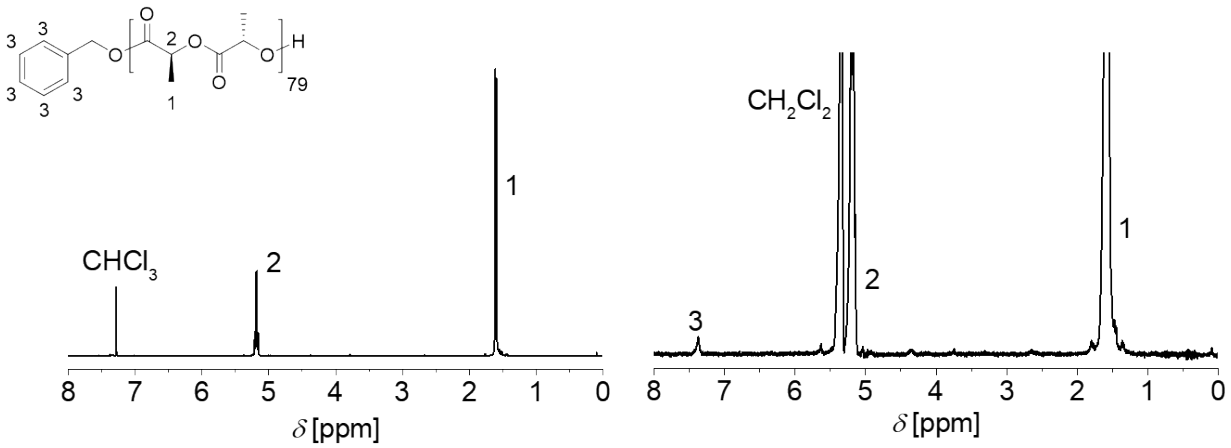


Figure S9: ^{1}H NMR characterization of PLLA (**P1**) and structural assignment of the signals. **Left**: ^{1}H NMR spectrum (400 MHz) in $CDCl_3$. **Right**: ^{1}H NMR spectrum (300 MHz) in CD_2Cl_2.

Poly(D-lactide) (**P2**):

800 mg D-Lactide (5.55 mmol) in 18.50 mL toluene and 111 µL stock solution containing 5.74 µL BnOH (0.06 mmol), 7.97 µL mTBD (0.06 mmol) and 97.29 µL toluene were used. The quenching was performed using 27.4 mg benzoic acid (0.22 mmol).

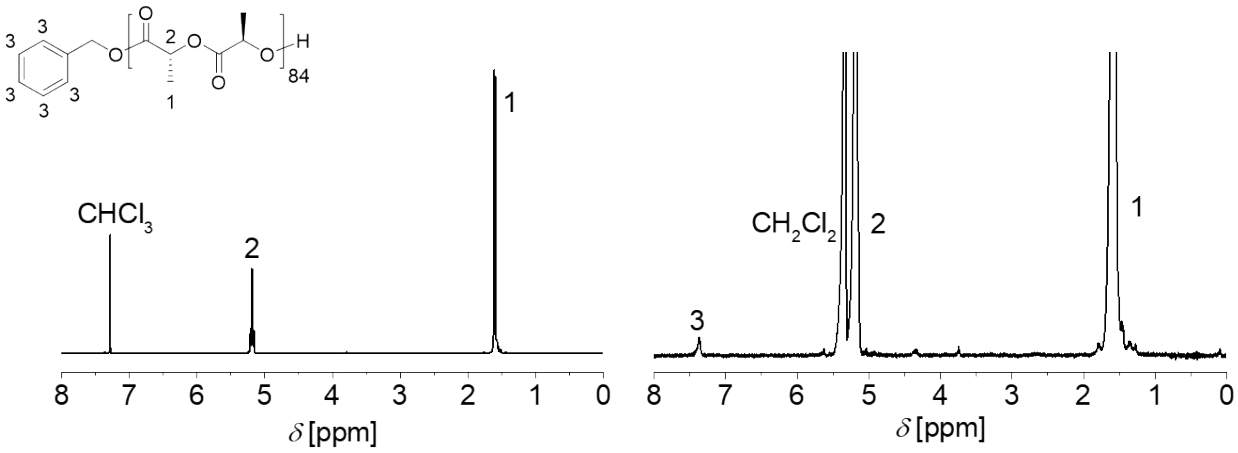


Figure S10: ^{1}H NMR characterization of PDLA (**P2**) and structural assignment of the signals. **Left**: ^{1}H NMR spectrum (400 MHz) in $CDCl_3$. **Right**: ^{1}H NMR spectrum (300 MHz) in CD_2Cl_2.

Poly(3-ethylglycolide) (**P3**):

535 mg EtGly (3.72 mmol) in 12.37 mL toluene and 74.24 µL stock solution consisting of 3.84 µL BnOH (0.04 mmol), 5.33 µL mTBD (0.04 mmol) and 65.07 µL toluene were utilized. The quenching was performed using 20.22 mg benzoic acid (0.17 mmol) dissolved in chloroform. Conversion was calculated from GC analysis.

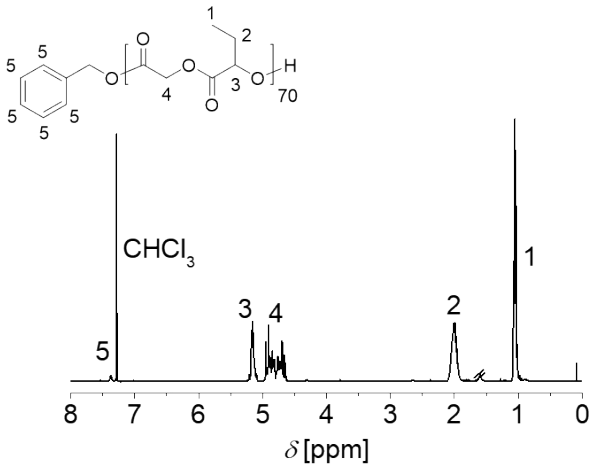


Figure S11: ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **P3** and structural assignment of the signals.

Poly(L-lactide-*stat*-3-ethylglycolide) (**P4**):

352 mg L-Lactide (2.44 mmol) and 19 mg EtGly (0.13 mmol) were used according to the general procedure in order to obtain a copolymer with 5% EtGly content.

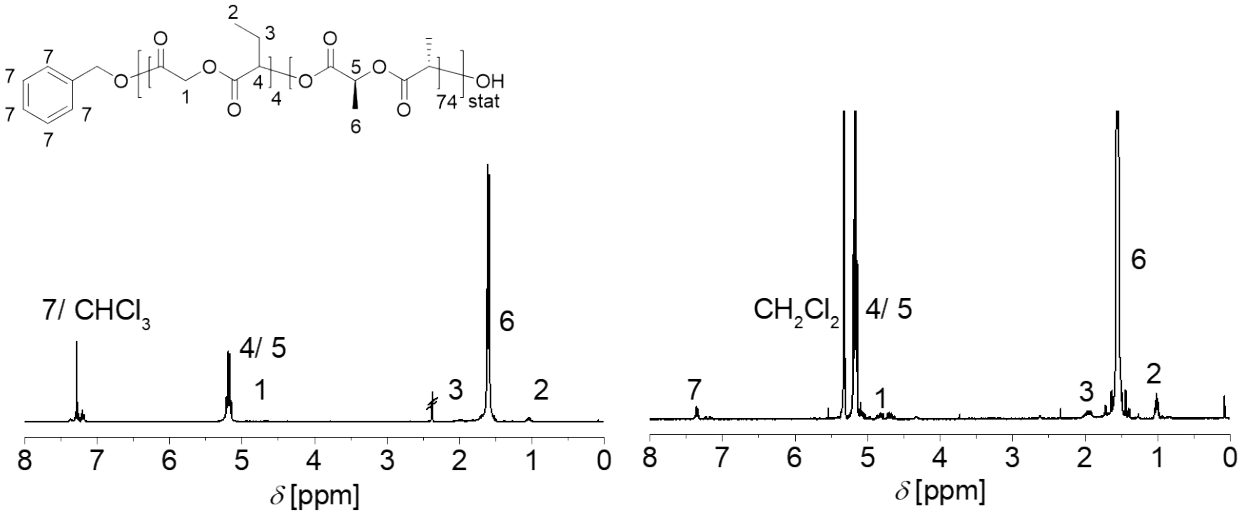


Figure S12: ^{1}H NMR characterization of **P4** and structural assignment of the signals. **Left**: ^{1}H NMR spectrum (300 MHz) in $CDCl_3$. **Right**: ^{1}H NMR spectrum (300 MHz) in CD_2Cl_2.

Poly(L-lactide-*stat*-3-ethylglycolide) (**P5**):

333 mg L-Lactide (2.31 mmol) and EtGly 37 mg (0.26 mmol) were used according to the general procedure in order to obtain a copolymer with 10% EtGly content.

P(LLA-*stat*-EtGly) (**P5**): feed LLA / EtGly = 90 / 10; conv = 74%; yield = 61%. ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 1.00 – 1.07 (br, 24H, H-2), 1.59 – 1.60 (br, 428H, H-6), 1.89 – 2.09 (br, 17H, H-3), 4.59 – 4.94 (br, 16H, H-1), 5.09 – 5.21 (br, 140H, H-4, H-5), ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.04 – 1.06 (br, 25H, H-2), 1.45 – 1.63 (br, 484H, H-6), 1.93 – 2.06. (br, 18H, H-3), 4.67 – 4.90 (br, 17H, H-1), 5.10 – 5.23 (br, 142H, H-4, H-5), 7.39 (br, 5H, H-7); SEC ($CHCl_3$, PS calibration): M_n = 13 kg mol^{-1}; $Đ$ = 1.20.

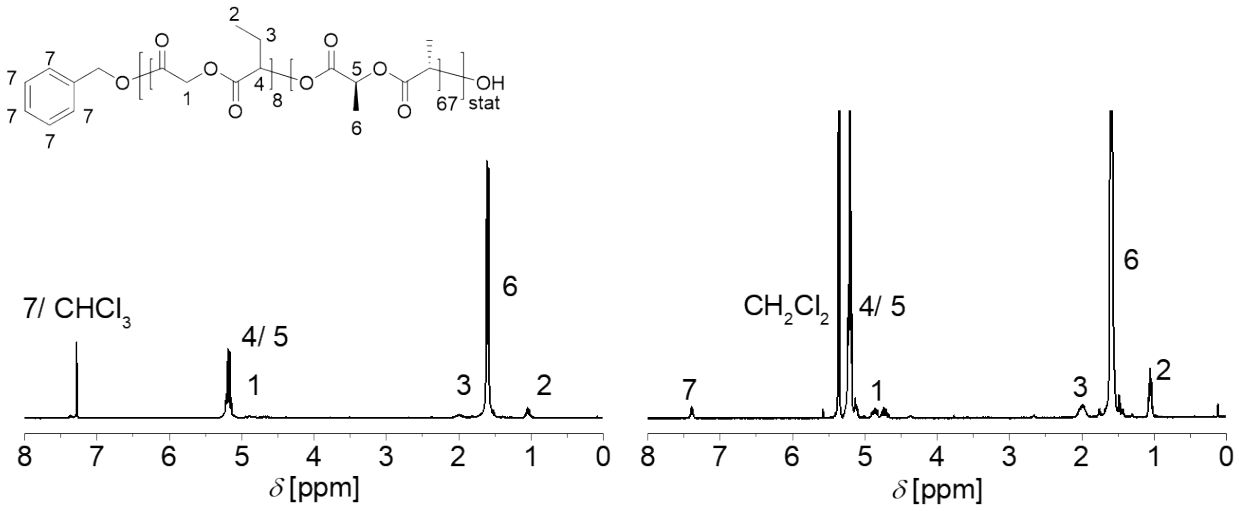


Figure S13: ^{1}H NMR characterization of **P5** and structural assignment of the signals. **Left**: ^{1}H NMR spectrum (300 MHz) in $CDCl_3$. **Right**: ^{1}H NMR spectrum (300 MHz) in CD_2Cl_2.

Poly(L-lactide-*stat*-3-ethylglycolide) (**P6**):

296 mg L-Lactide (2.05 mmol) and 74.0 mg EtGly (0.51 mmol) were used according to the general procedure in order to obtain a copolymer with 20% EtGly content.

P(LLA-*stat*-EtGly) (**P6**): feed LLA / EtGly = 80 / 20; conv = 69%; yield = 61 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 1.00 – 1.07 (br, 45H, H-2), 1.50 – 1.61 (br, 336H, H-6), 1.91 – 2.06 (br, 32H, H-3), 4.59 – 4.94 (br, 30H, H-1), 5.10 – 5.24 (br, 120H, H-4, H-5), ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.04 – 1.07 (br, 46H, H-2), 1.47 – 1.60 (br, 373H, H-6), 1.93 – 2.08. (br, 32H, H-3), 4.67 – 4.91 (br, 30H, H-1), 5.12 – 5.23 (br, 119H, H-4, H-5), 7.40 (br, 5H, H-7); SEC ($CHCl_3$, PS calibration): M_n = 12 kg mol^{-1}; $Đ$ = 1.23.

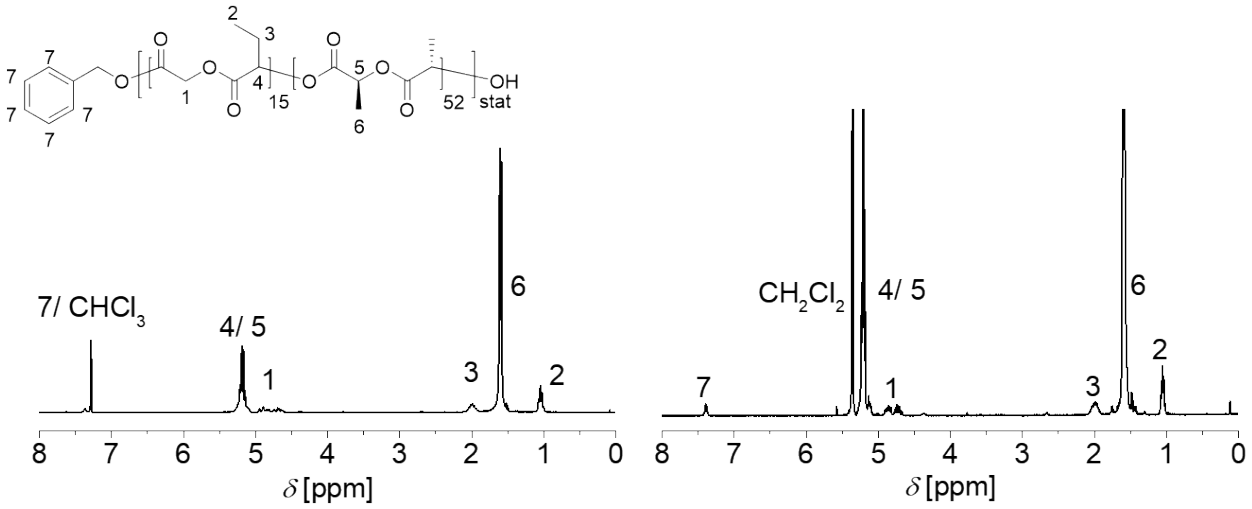


Figure S14: ^{1}H NMR characterization of **P6** and structural assignment of the signals. **Left**: ^{1}H NMR spectrum (300 MHz) in $CDCl_3$. **Right**: ^{1}H NMR spectrum (300 MHz) in CD_2Cl_2.

Poly(L-lactide-*stat*-3-ethylglycolide) (**P7**):

352 mg D-Lactide (2.44 mmol) and 19 mg EtGly (0.13 mmol) were used according to the general procedure in order to obtain a copolymer with 5% EtGly content.

P(DLA-*stat*-EtGly) (**P7**): feed DLA / EtGly = 95 / 05; conv = 77%; yield = 72%. ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 1.02 – 1.07 (br, 9H, H-2), 1.50 – 1.71 (br, 461H, H-6), 1.89 – 2.06 (br, 7H, H-3), 4.59 – 4.94 (br, 6H, H-1), 5.10 – 5.21 (br, 145H, H-4, H-5), ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.04 – 1.06 (br, 11H, H-2), 1.47 – 1.60 (br, 555H, H-6), 1.93 – 2.08. (br, 8H, H-3), 4.67 – 4.91 (br, 7H, H-1), 5.13 – 5.23 (br, 157H, H-4, H-5), 7.40 (br, 5H, H-7); SEC ($CHCl_3$, PS calibration): M_n = 19 kg mol^{-1}; $Đ$ = 1.10.

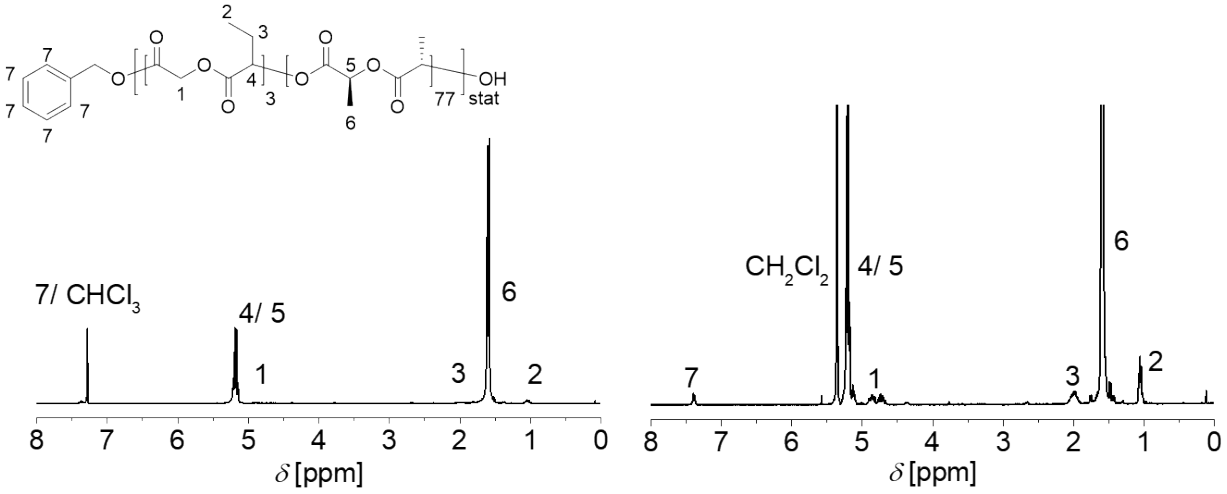


Figure S15: ^{1}H NMR characterization of **P7** and structural assignment of the signals. **Left**: ^{1}H NMR spectrum (300 MHz) in $CDCl_3$. **Right**: ^{1}H NMR spectrum (300 MHz) in CD_2Cl_2.

Poly(L-lactide-*stat*-3-ethylglycolide) (**P8**):

333 mg D-Lactide (2.31 mmol) and 37 mg EtGly (0.26 mmol) were used according to the general procedure in order to obtain a copolymer with 10% EtGly content.

P(DLA-*stat*- EtGly) (**P8**): feed DLA / EtGly = 90 / 10; conv = 79%; yield = 71%. ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 0.96 – 1.07 (br, 21H, H-2), 1.47 – 1.80 (br, 450, H-6), 1.92 -2.07 (br, 16H, H-3), 4.59 – 4.94 (br, 14H, H-1), 5.10 – 5.21 (br, 145H, H-4, H-5), ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.04 – 1.06 (br, 23H, H-2), 1.49 – 1.60 (br, 513H, H-6), 1.92 – 2.08. (br, 16H, H-3), 4.67 – 4.91 (br, 14H, H-1), 5.10 – 5.23 (br, 149H, H-4, H-5), 7.39 (br, 5H, H-7); SEC ($CHCl_3$, PS calibration): M_n = 18 kg mol^{-1}; $Đ$ = 1.21.

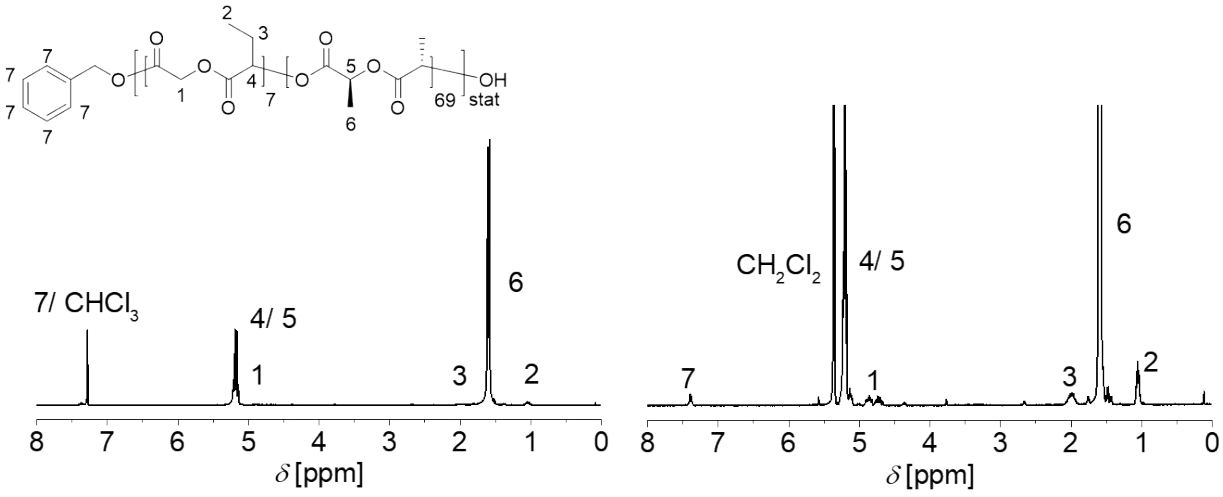


Figure S16: ^{1}H NMR characterization of **P8** and structural assignment of the signals. **Left**: ^{1}H NMR spectrum (300 MHz) in $CDCl_3$. **Right**: ^{1}H NMR spectrum (300 MHz) in CD_2Cl_2.

Poly(L-lactide-*stat*-3-ethylglycolide) (**P9**):

296 mg D-Lactide (2.05 mmol) and 74.0 mg EtGly (0.51 mmol) were used according to the general procedure in order to obtain a copolymer with 20% EtGly content.

P(DLA-*stat*-EtGly) (**P9**): feed DLA / EtGly = 80 / 20; conv = 77%; yield = 63%. ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 1.00 – 1.07 (br, 48H, H-2), 1.50 – 1.80 (br, 354, H-6), 1.92 – 2.09 (br, 32H, H-3), 4.59 – 4.94 (br, 31H, H-1), 5.11 – 5.21 (br, 123H, H-4, H-5), ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.04 – 1.07 (br, 51H, H-2), 1.47 – 1.60 (br, 426H, H-6), 1.93 – 2.08. (br, 36H, H-3), 4.67 – 4.91 (br, 32H, H-1), 5.11 – 5.23 (br, 129H, H-4, H-5), 7.40 (br, 5H, H-7); SEC ($CHCl_3$, PS calibration): M_n = 15 kg mol^{-1}; $Đ$ = 1.28.

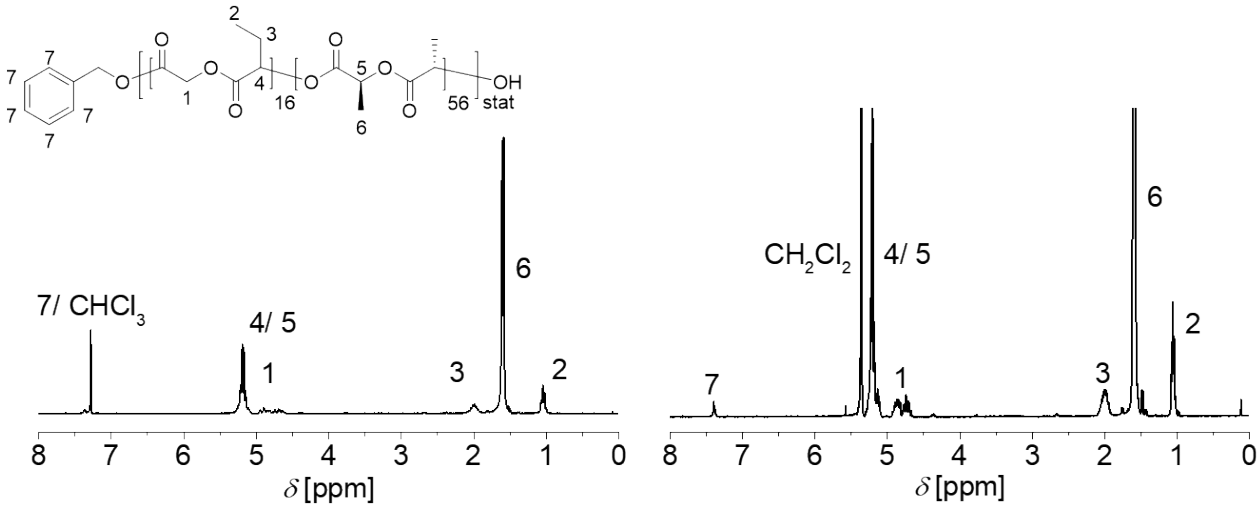


Figure S17: ^{1}H NMR characterization of **P9** and structural assignment of the signals. **Left**: ^{1}H NMR spectrum (300 MHz) in $CDCl_3$. **Right**: ^{1}H NMR spectrum (300 MHz) in CD_2Cl_2.

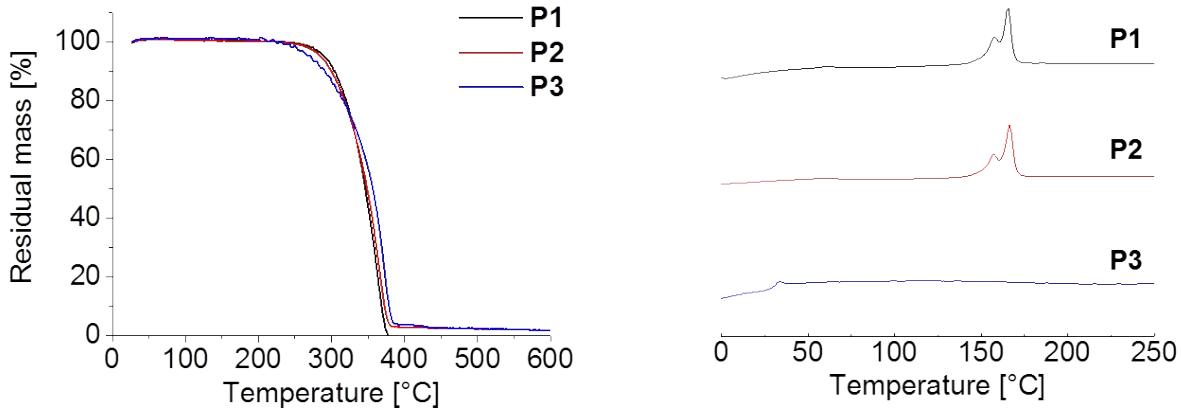


Figure S18: Thermal analysis of the homopolymers **P1** to **P3**. **Left**: TGA thermograms (nitrogen atmosphere, heating rate 20 K min^{-1}). **Right**: DSC thermograms from the first heating run (from – 20 to 260 °C, heating rate 20 K min^{-1}).

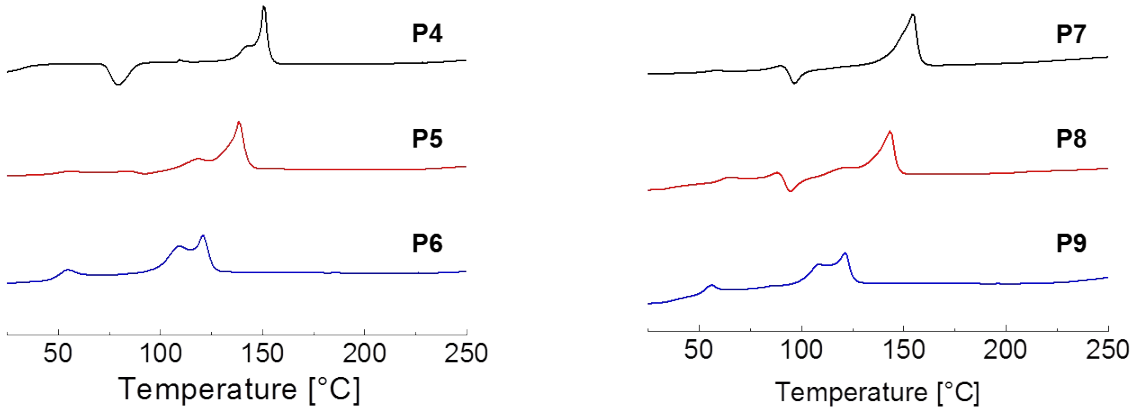


Figure S19: DSC thermograms of the copolyesters. The measurements were performed from –20 to 260 °C (first heating run, heating rate 20 K min^{-1}, cooling rate 20 K min^{-1}). **Left**: **P4** to **P6** based on PLLA. **Right**: **P7** to **P9** based on PDLA.

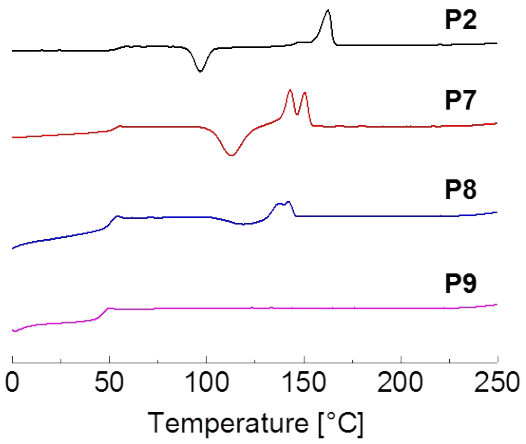


Figure S20: DSC thermograms of the PDLA based polyesters **P2** and **P7** to **P9**. The measurements were performed from –20 to 260 °C (third heating run, heating rate 10 K min^{-1}, cooling rate 20 K min^{-1}).

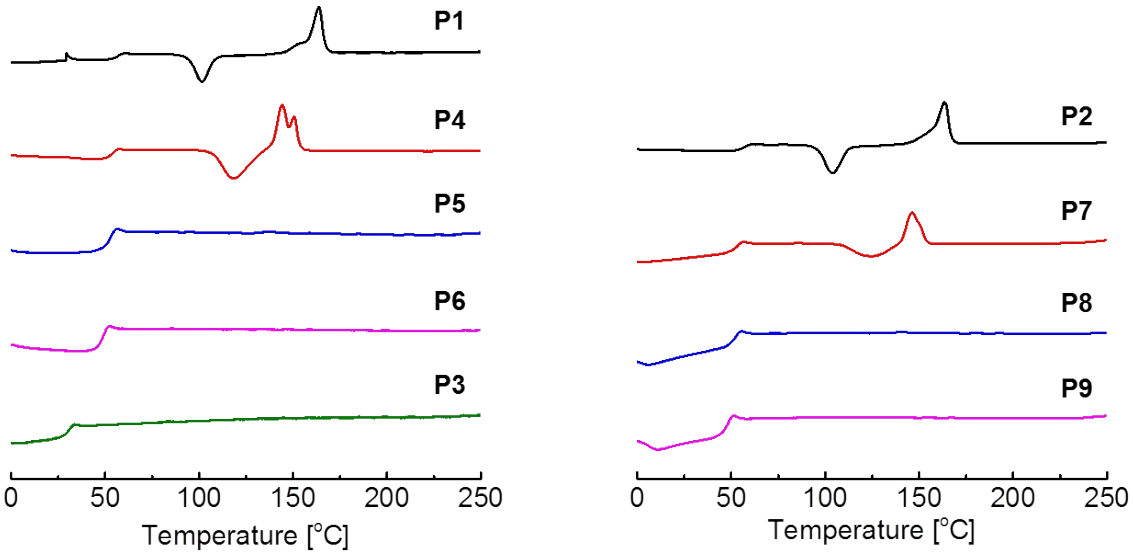


Figure S21: DSC thermograms of **P1** to **P9**. **Left**: PLLA based polyesters. **Right**: PDLA based polyesters. The measurements were performed from –20 to 260 °C (second heating run, heating rate 20 K min^{-1}, cooling rate 20 K min^{-1}).

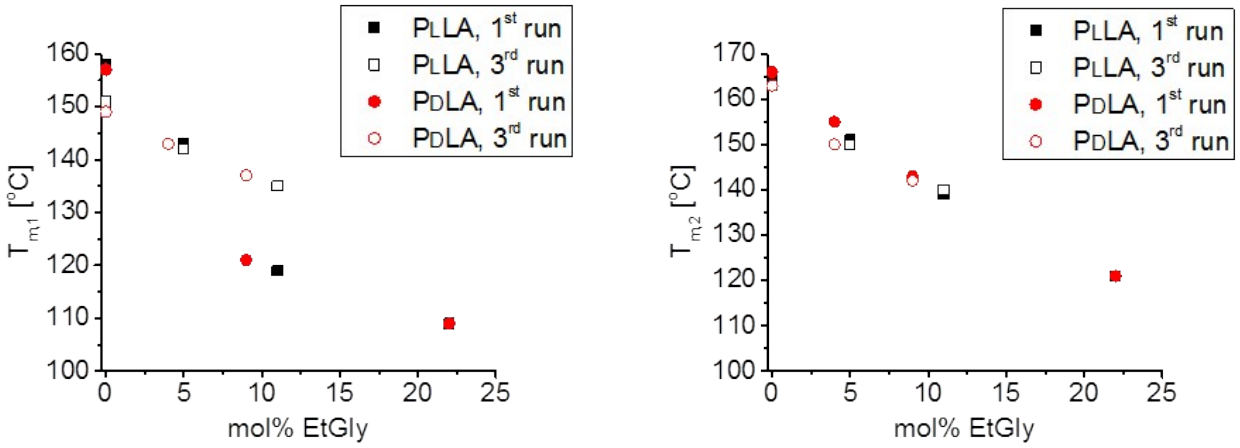


Figure S22: Influence of the molar fraction of EtGly on the melting temperatures of the copolyester series based on PLLA (**P1**, **P3** to **P6**) and on PDLA (**P2**, **P7** to **P9**) as determined *via* DSC analysis (cooling rates: 20 K min^{-1}, heating rate in the first run: 20 K min^{-1}, heating rate in the third run: 10 K min^{-1}). **Left**: First event of fusion ($T_{m,1}$). **Right**: Second event of fusion ($T_{m,2}$).

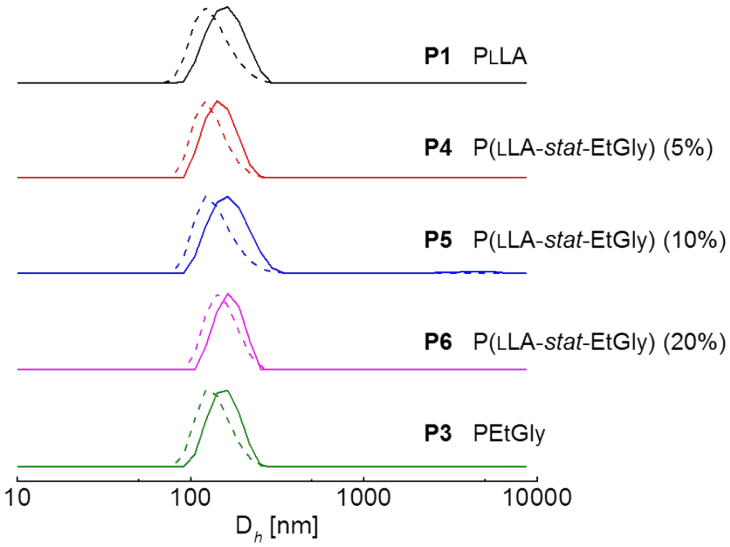


Figure S23: DLS size distributions of the nanoparticles prepared from **P1** and **P3** to **P6** with hydrodynamic diameters of $D_h \approx 150$ nm. The full lines represent the intensity weighted data, the dotted lines represent the number weighted data.

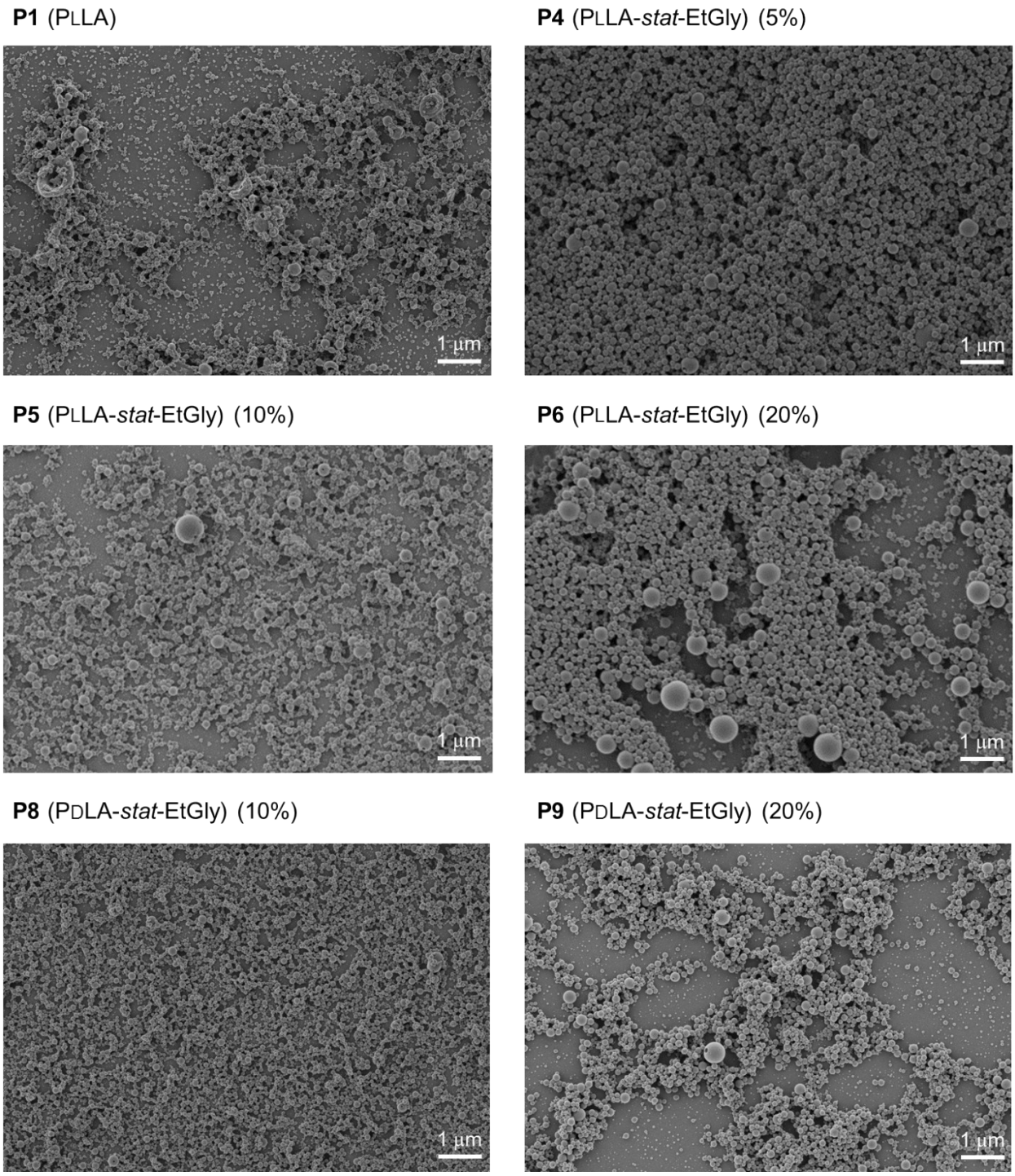


Figure S24: SEM images of dried nanoparticles prepared by nanoprecipitation. Scale bars represent 1 µm.

Table S3: Summary of nanoparticle size distributions, ζ-potential and fluorescence band ratio of the pyrene (Py) loaded nanoparticles.

Polymer	c(**P1** to **P3**) in THF [mg mL^{-1}]	c(Py) in THF [mg mL^{-1}]	c(**P1** to **P3**) in H_2O [mg mL^{-1}]	c(Py) in H_2O [mg mL^{-1}]	ζ [mV]	D_h [nm]	PDI	I_1 / I_3[1]
P1	4.75	0.05	0.475	0.005	–33	149	0.13	1.26
P2	4.75	0.05	0.475	0.005	–39	149	0.11	1.29
P3	1.425	0.015	0.1425	0.0015	–33	171	0.20	1.25

[1] Fluorescence spectra recorded using 100 fold diluted nanoparticle suspensions.

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