

Supporting Information

Introducing an Amine Functionality at the Block Junction of Amphiphilic Block Copolymers by Anionic Polymerization Strategies

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Experimental Section

Reagents

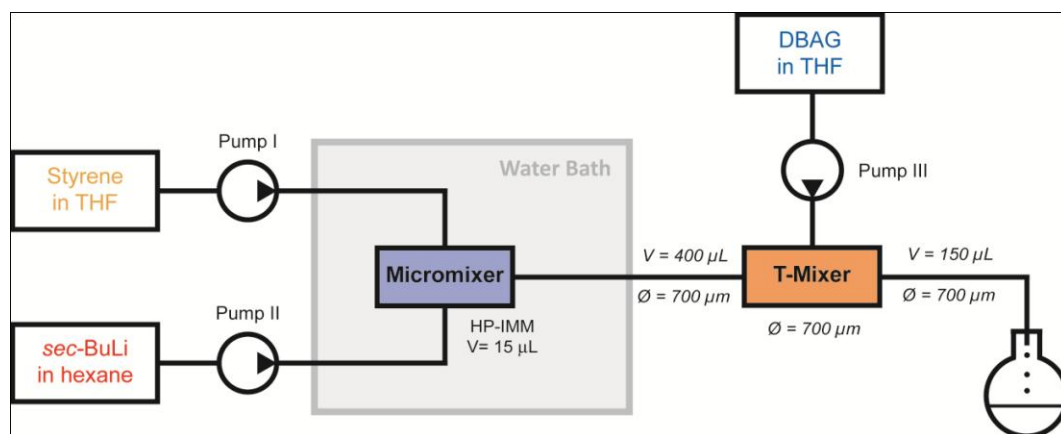
All solvents and reagents were purchased from Acros Organics or Sigma Aldrich and used as received unless otherwise stated. Chloroform-*d*₁ was purchased from Deutero GmbH. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under reduced pressure (cryo-transfer). Styrene was dried over calcium hydride (CaH₂) and cryo-transferred prior to use. Cyclohexane was cryo-transferred from *n*-buthyllithium/DPE. *sec*-Butyllithium (*sec*-BuLi, 1,3 M, Acros) was used as received and the concentration of the initiator was determined by the Gilman double titration method.¹ *N,N*-Dibenzyl amino glycidol (DBAG) was synthesized as reported previously.²

Instrumentation

¹H NMR spectra were recorded at 300 MHz or 400 MHz on a Bruker AC300 or Bruker AMX 400 respectively and were referenced internally to residual proton signals of the deuterated solvent. Size exclusion chromatography (SEC) measurements were carried out in THF or CHCl₃ on an instrument consisting of a Waters 717 plus auto sampler, a TSP Spectra Series P 100 pump, a set of three PSS SDV columns (104/500/50 Å), RI- and UV-detectors (absorption wavelength: 254 nm or 500 nm). All SEC diagrams show the RI detector signal unless otherwise stated, and the molecular weight refer to linear polystyrene (PS) standards provided by Polymer Standards Service (PSS). Matrix-assisted laser desorption/ionization time-of-flight (MALDI-ToF) measurements were performed on a Shimadzu Axima CFR MALDI-TOF mass spectrometer using silver trifluoroacetate as cationizing agent and dithranol (1,8,9-trihydroxy-anthracene) as a matrix. UV/vis spectroscopy was measured on a JASCO V-630 UV-VIS spectrophotometer and fluorescence was accomplished on a JASCO PL 6200 spectrofluorometer.

Microstructured Reactor

A continuous flow reaction setup (Scheme S1) equipped with a micromixer was employed for the synthesis of DBAG-functionalized polystyrene as reported previously.³ A stainless steel high pressure slit interdigital micromixer (HP-IMM, provided by the Institut für Mikrotechnik Mainz (IMM)) with an internal volume of 15 μL was used for fast and efficient mixing of monomer and initiator realized by multilamination mixing mode, combined with geometric and hydrodynamic focusing.⁴ The micromixer was immersed in a tempered water bath (room temperature) and equipped with two reactant inlets and one outlet. After mixing of monomer and initiator (within several milliseconds), the reaction mixture passed a short stainless steel capillary residence tube and was combined with DBAG (separate flow tube) in a T-mixer ($\varnothing = 700 \mu\text{m}$). The residence tube behind the T-mixer was connected to a degassed vessel for sample collection. Flow rates were controlled via HPLC pumps (Knauer WellChrom K-501, inert 10 mL pump heads with ceramic inlays).



Scheme S1: Schematic reactor setup continuous polymerization-termination processes. Monomer: styrene; initiator: *sec*-BuLi; capping reagent: DBAG; micromixer: HP-IMM.

Continuous Synthesis of PS-DBAG

Exemplary synthesis procedure for PS₃₃-(DBAG) (#S2 Table S1): Prior to the polymerization reaction, THF was pumped through the microstructured reactor setup (Scheme S1) for 10 min with a flow rate of 0.5 mL·min⁻¹ at each HPLC pump to rinse off residual impurities. A solution of purified styrene (1.47 M) in dry THF was kept under argon in a flask covered with a septum. Into a second flask equipped with dry hexane, 4.0 mL *sec*-BuLi was added via syringe directly before starting the reaction (0.05 M). The third flask contained a solution of purified DBAG in THF (0.1 M). The three flasks were connected to the HPLC pumps via PTFE tubes transfixed through the septa. To eliminate residual impurities prior to the polymerization start, pump II was activated and the assembly was flushed with the *sec*-BuLi solution. In order to initiate the continuous process, pumps I (monomer) and II (initiator) were activated each with flow rates of 1 mL·min⁻¹. After the characteristic reddish color appeared at the outlet, pump III was activated with a flow rate of 1 mL·min⁻¹ to combine the DBAG-

solution and the living polystyrene within the T-mixer. Full monomer conversion was achieved after 12 s, and the end-capped polymer was recovered from a short outlet tube connected to the T-junction. PS₃₃-DBAG was precipitated several times in methanol to remove residual DBAG. The final product was dried in vacuum at room temperature for 12 h. All polymer samples (Table S1) prepared by the continuous end capping process have been produced by an analogous procedure. Adjusting the flow rate via the control elements of the HPLC pumps or using different concentrations permits convenient variation of molecular weight. ¹H NMR (400 MHz, CDCl₃, δ in ppm): 7.50-6.18 (PS aromatic), 3.66 (m, 2H, CH₂-Ph), 3.48-3.20 (m, 3H, CH₂-Ph, CH-OH), 2.6-0.80 (PS backbone), 0.79-0.50 (m, 6H, (CH₃-CH₂-CH-CH₃)). ¹³C NMR (100 MHz, CDCl₃, δ in ppm): 145.5 (PS aromatic.), 138.46 (aromatic Carbon subst. protecting group), 128.0 (PS aromatic), 125.6 (PS aromatic), 64.6 (CH-OH), 60.2-58.9 (CH₂-NR₂), 58.2 (N-(CH₂)₂), 47.1-41.0 (CH₂ backbone), 40.3 (CH backbone), 31.5 (CH₃-CH), 29.9 (CH₃-CH), 18.5 (CH₃), 11.2 (CH₃).

Table S1: Characterization data of PS-DBAG samples synthesized in continuous flow.

#	Polymer ^a	M _n ^b	PDI ^b
1 ^c	PS ₂₀ -(DBAG)	2200	1.19
2 ^c	PS ₄₅ -(DBAG)	5000	1.18
3 ^c	PS ₁₂₂ -(DBAG)	13000	1.12
4 ^c	PS ₁₉₉ -(DBAG)	20000	1.19
S1	PS ₂₇ -(DBAG)	3100	1.25
S2	PS ₃₃ -(DBAG)	3700	1.19
S3	PS ₃₄ -(DBAG)	3700	1.17
S4	PS ₃₇ -(DBAG)	3800	1.15
S5	PS ₅₂ -(DBAG)	5900	1.15
S6	PS ₆₈ -(DBAG)	7500	1.15
S7	PS ₇₄ -(DBAG)	8200	1.14

^acalculated by ¹H NMR, ^bmolecular weight in g/mol and MWD characterized by SEC in THF (PS-Standard),

^calready listed in the main publication (Table 1).

Conventional Procedure for PS-DBAG

Vacuum-distilled styrene (5 g, 48 mmol) was dissolved in dry cyclohexane (30 mL), cooled to 0 °C and the polymerization was initiated with the corresponding amount of *sec*-BuLi (1.3 M, 1.28 mL). The red-colored reaction mixture was stirred for 20 h at 40 °C. After a small amount of THF (~1-2 mL) was cryo-transferred to the reaction mixture, DBAG (2 eq.) was introduced via syringe to terminate the polymerization and the dark red color disappeared immediately. The solution was stirred for further 20 h and precipitated several times into MeOH to obtain 5 g (90%) PS-DBAG (**2**). ¹H NMR (400 MHz, CDCl₃, δ in ppm): 7.50-6.18 (PS aromatic), 7.32 (m, 4H, meta- of protective benzyl groups), 3.66 (m, 2H, CH₂-Ph), 3.48-3.20 (m, 3H, CH₂-Ph, CH-OH), 2.6-0.80 (PS backbone), 0.79-0.50 (m, 6H,

($\text{CH}_3\text{-CH}_2\text{-CH-CH}_3$). ^{13}C NMR (100 MHz, CDCl_3 , δ in ppm): 145.5 (PS aromatic.), 138.5 (aromatic, protecting group), 129.0-125.0 (PS aromatic), 64.6 (CH-OH), 60.2-58.9 ($\text{CH}_2\text{-NR}_2$), 58.2 (N-(CH_2) $_2$), 47.1-41.0 (CH_2 backbone), 40.3 (CH backbone), 31.5 ($\text{CH}_3\text{-CH}$), 29.9 ($\text{CH}_3\text{-CH}$), 18.5 (CH_3), 11.2 (CH_3).

Synthesis of PS-(DBAG)-*b*-PEO

500 mg PS-DBAG (#6) were dissolved in dry THF in a 100 mL Schlenk flask and titrated with potassium naphthalide (0.1 M) until a slight green color maintained. The monomer ethylene oxide (EO, 1 mL) was cryo-transferred into a graduated ampoule and subsequently into the reaction flask at approximately $-80\text{ }^\circ\text{C}$. The greenish color disappeared rapidly. The reaction mixture was heated up to $60\text{ }^\circ\text{C}$ and stirred for 24 h. The polymerization was terminated with either degassed methanol or freshly distilled allyl bromide (2 eq.) and precipitated in cold diethyl ether. Drying in vacuum at room temperature leads to 1.3 g PS-(DBAG)-*b*-PEO. Yield: 94 %. ^1H NMR (400 MHz, CDCl_3 , δ in ppm): 7.35-6.24 (PS aromatic), 7.22 (m, 4H, meta- of protective benzyl groups), 5.90^a (m, 1H, $\text{CH}_2\text{-CH=CH}_2$), 5.26^a (dq, 1H, CH=CH_2), 5.17^a (dq, 1H, CH=CH_2), 4.02^a (dt, 2H, $\text{CH}_2\text{-CH=CH}_2$), 3.86-3.38 (PEO backbone), 2.5-0.80 (PS backbone), 0.79-0.50 (m, 6H, ($\text{CH}_3\text{-CH}_2\text{-CH-CH}_3$)). ^{13}C NMR (100 MHz, CDCl_3 , δ in ppm): 145.1 (PS aromatic.), 139.3 (aromatic, protecting group), 134.7^a ($\text{CH}_2\text{-CH=CH}_2$), 128.7-125.5 (PS aromatic), 117.0^a (CH=CH_2), 72.1 (CH-OH), 70.5 (PEO backbone), 69.3 (Core-PEO- CH_2) 61.1^b ($\text{CH}_2\text{-OH}$) 59.5-59.1 ($\text{CH}_2\text{-NR}_2$), 59.0 (N-(CH_2) $_2$), 47.1-41.0 (PS- CH_2 backbone), 40.3 (PS-CH backbone).

^aallyl bromide-terminated polymers, ^bmethanol-terminated polymers.

Synthesis of PS-(NH₂)-*b*-PEO

Catalytic hydrogenolysis of PS-(DBAG)-*b*-PEO was carried out as described previously.² The polymer (500 mg) was dissolved in a solvent mixture of 40 mL of THF, 20 mL of MeOH and 20 mL of H_2O (2:1:1) and 100 mg palladium hydroxide (10-20 wt%) on activated carbon ($\text{Pd(OH)}_2/\text{C}$) were added. The reaction mixture was stirred for 5 days at 40 bar H_2 . After removal of the catalyst by filtration over Celite and removal of solvent under reduced pressure PS-(NH₂)-*b*-PEO was obtained. Strong adhesion of the amphiphilic block copolymer as well as the amino function to $\text{Pd(OH)}_2/\text{C}$ resulted in yields of 50-70%. ^1H NMR (400 MHz, CDCl_3 , δ in ppm): 7.35-6.24 (PS aromatic), 4.05-3.29 (PEO backbone), 2.5-0.80 (PS backbone), 0.79-0.50 (m, 6H, ($\text{CH}_3\text{-CH}_2\text{-CH-CH}_3$)). ^{13}C NMR (100 MHz, CDCl_3 δ in ppm): 145.3 (PS aromatic), 128.9-125.5 (PS aromatic), 73.0 ($\text{CH-CH}_2\text{-NH}_2$), 70.5 (PEO backbone), 49.8 ($\text{CH}_2\text{-NH}_2$), 47.1-41.0 (PS- CH_2 backbone), 40.2 (PS-CH backbone).

Synthesis of NHS-FI

2-(6-Hydroxy-3-oxo-3*H*-xanthen-9-yl)-benzoic acid 2,5-dioxo-pyrrolidin-1-yl ester (*N*-hydroxysuccinimide ester of fluorescein) was synthesized as reported previously.⁵ The

reduced DMF solution was purified by flash chromatography using first petrol ether/ethyl acetat (20:80) and then MeOH/CHCl₃(30:70). ¹H NMR (300 MHz, DMSO-*d*₆, δ in ppm): 8.35 (d, 1H), 8.08-7.84 (m, 2H), 7.67 (d, 1H), 6.78 (d, 2H), 6.67-6.44 (m, 4H), 2.72 (s, 4H).

Synthesis PS-(NH-FI)-*b*-PEO

50 mg ($4 \cdot 10^{-3}$ mmol) PS-(NH₂)-*b*-PEO was dissolved in 5 mL of DMF. 2.6 mg ($6 \cdot 10^{-3}$ mmol, 1.5 eq.) NHS-FI and triethylamine (TEA) were added and the reddish reaction mixture was stirred for 24 h. The reaction was neutralized with acetic acid and purified by preparative chromatography (solvent: CHCl₃). Yield: 30 mg (58%). ¹H NMR (300 MHz, DMSO-*d*₆, δ in ppm): 7.44-6.29 (PS aromatic), 4.05-3.23 (PEO backbone), 2.5-0.77 (PS backbone), 0.79-0.5 (m, 6H, (CH₃-CH₂-CH-CH₃)).

UV/vis and Fluorescence Spectroscopy

The investigation of PS-(NH-FI)-*b*-PEO (#19), NHS-FI and a mixture of NHS-FI and PS-(DBAG)-*b*-PEO (#12) was started with the measurement of absorption spectra to indentify the maximum transition wavelength of each sample (Table S2). This wavelength was adjusted as excitation wavelength for fluorescence measurements. All samples were measured in ethanol solution ($2 \cdot 10^{-4}$ M) and Table S2 presents absorption as well as fluorescence maxima.

Table S2: Maxima of absorption and fluorecence measurements.

Sample	$\lambda_{\text{abs}}^{\text{a}}$	$\lambda_{\text{fl}}^{\text{b}}$
NHS-FI	511	535
PS-(NH-FI)- <i>b</i> -PEO	490	519
PS-(DBAG)- <i>b</i> -PEO /NHS-FI	512	536

^amaximum of absorption spectrum in nm, ^bmaximum of fluorescence spectrum in nm.

Additional Characterization Spectra

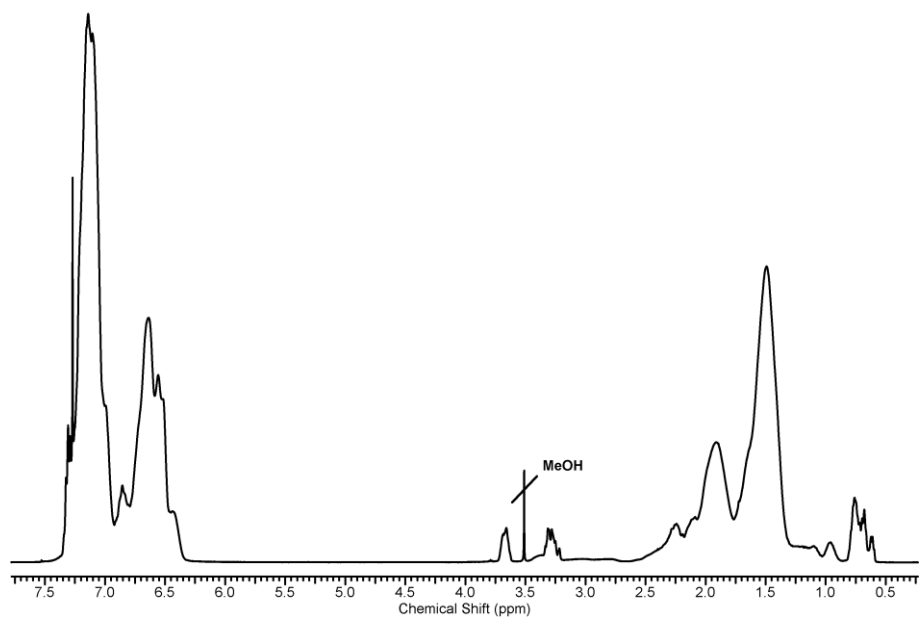


Fig. S 1: ¹H NMR spectrum of PS-DBAG (#6)

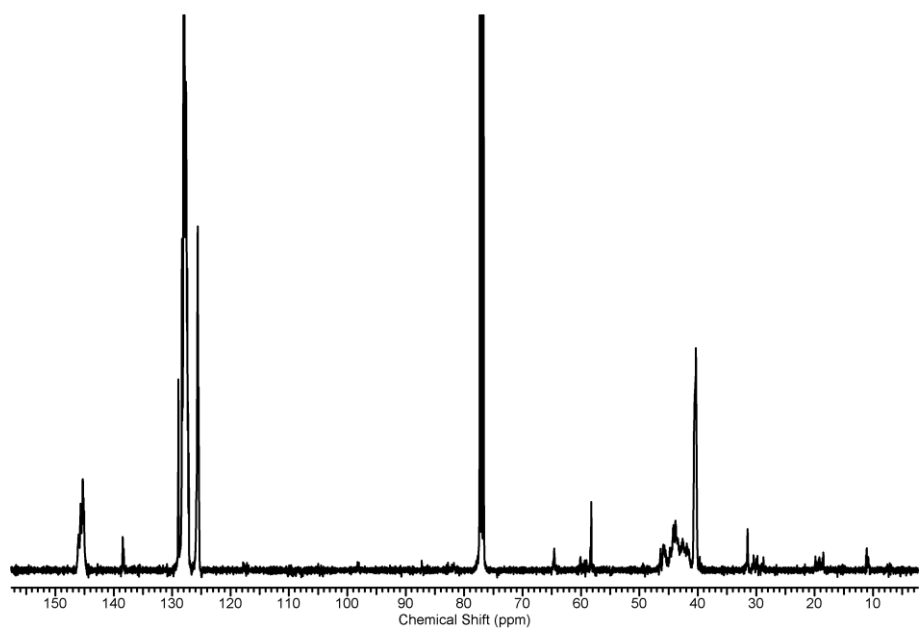


Fig. S 2: ¹³C NMR spectrum of PS-DBAG (#6)

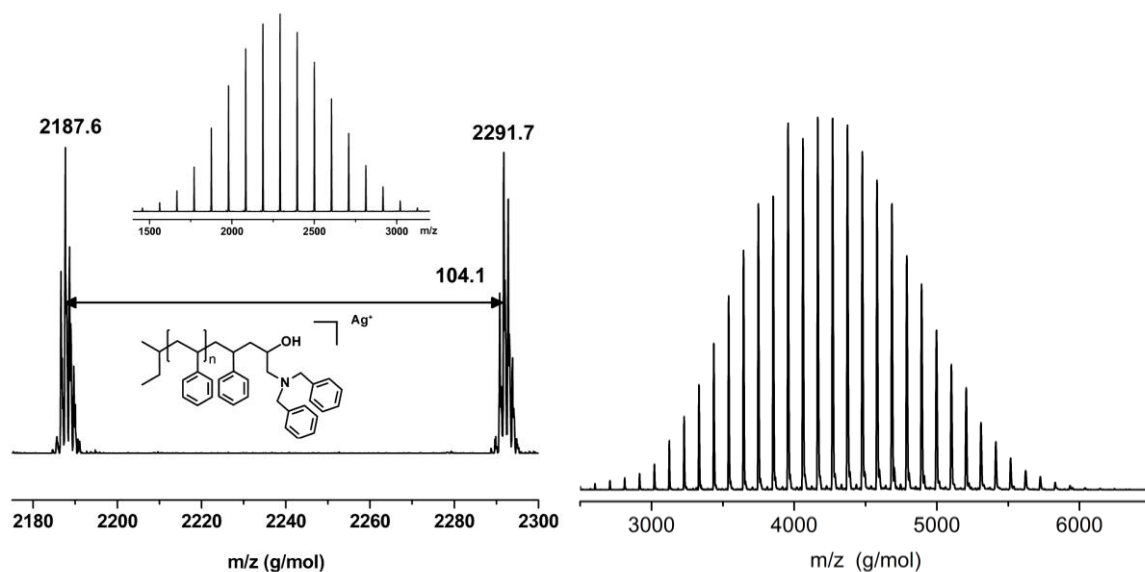


Fig. S 3: MALDI-ToF spectra of PS-DBAG synthesized via conventional procedure. Left spectra: #5 with enlarged region, right spectra: #7. Cationizing agent: silver trifluoro acetate, matrix: dithranol.

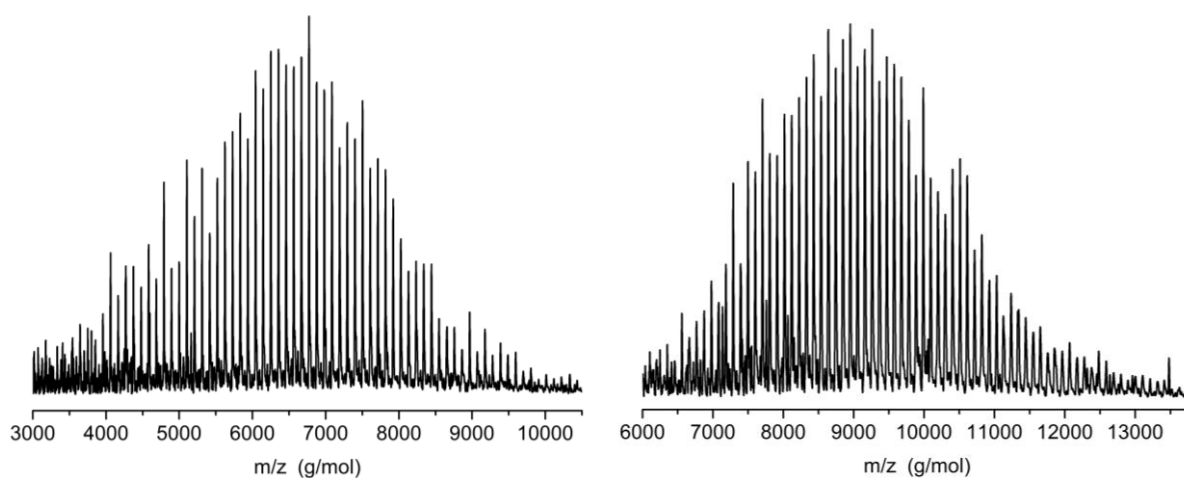


Fig. S 4: MALDI-ToF spectra of PS-DBAG synthesized in continuous flow. Left spectra: #S6 in Table S1, right spectra: #3. Cationizing agent: silver trifluoro acetate, matrix: dithranol.

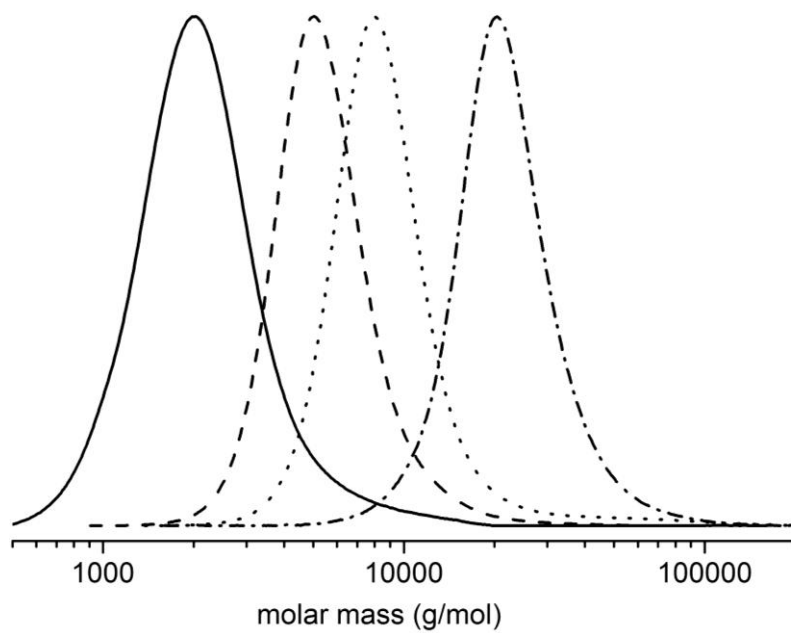


Fig. S 5: SEC traces of PS-DBAG (continuous procedure): #1 (solid line), #2 (dashed line), #S6 (dotted line) and #4 (dashed/dotted line).

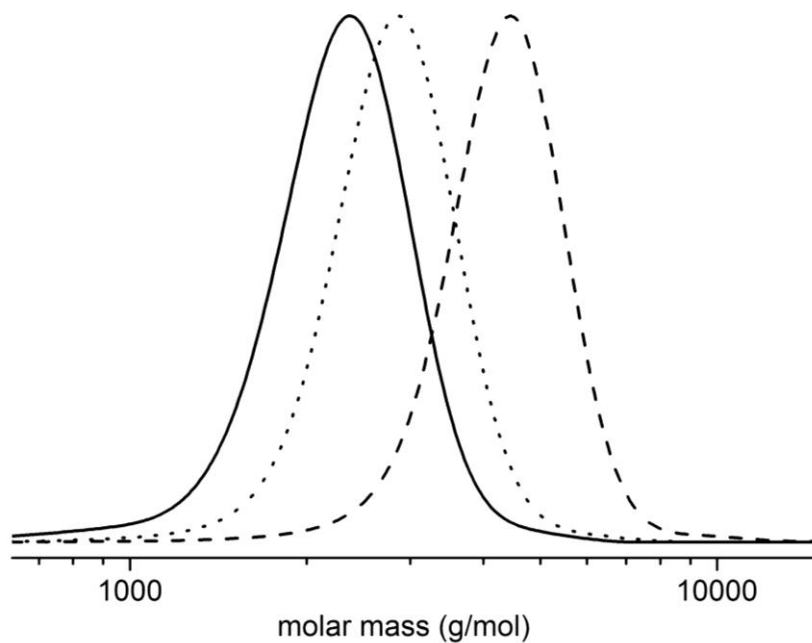


Fig. S 6: SEC traces of PS-DBAG (conventional procedure): #5 (solid line), #6 (dotted line), #7 (dashed line).

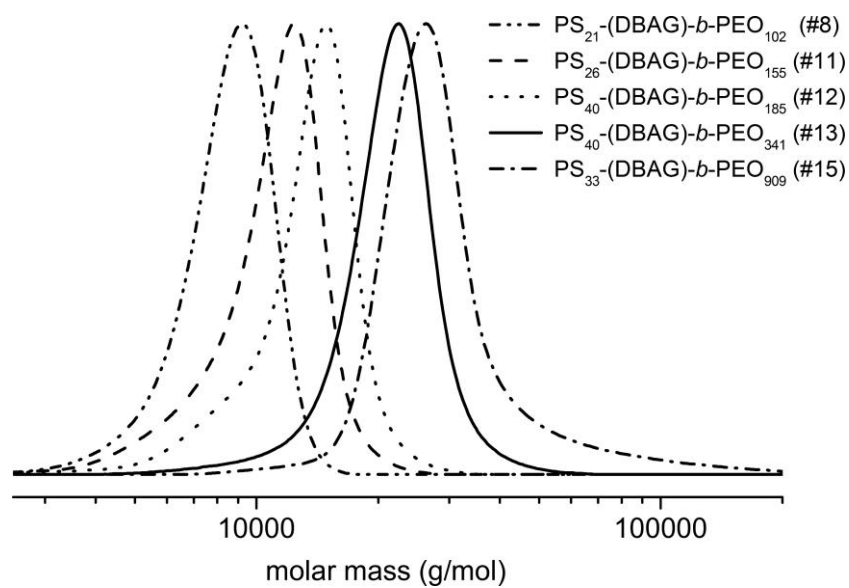


Fig. S 7: SEC traces of PS-(DBAG)-*b*-PEO.

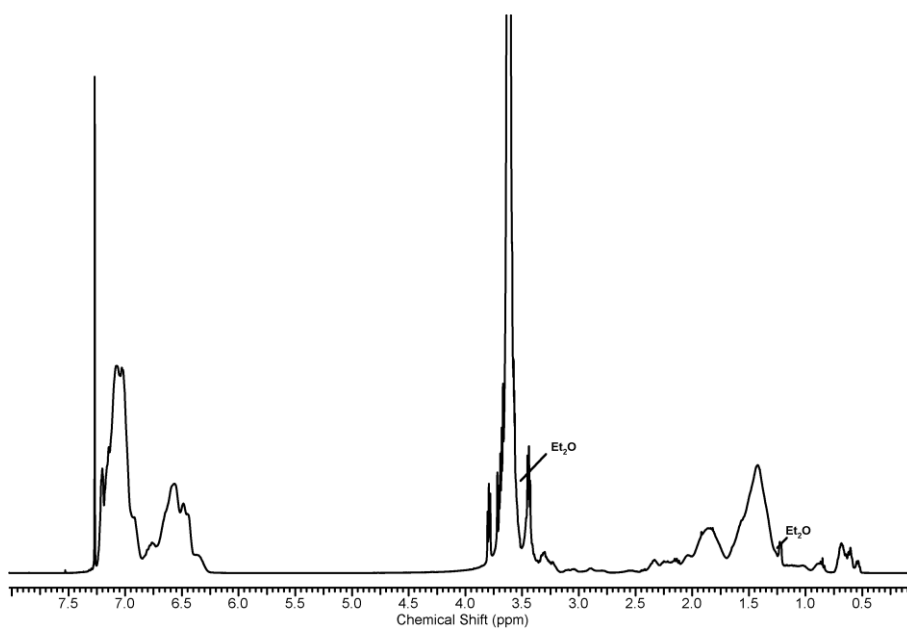


Fig. S 8: ¹H NMR spectrum of PS-DBAG-*b*-PEO (#10).

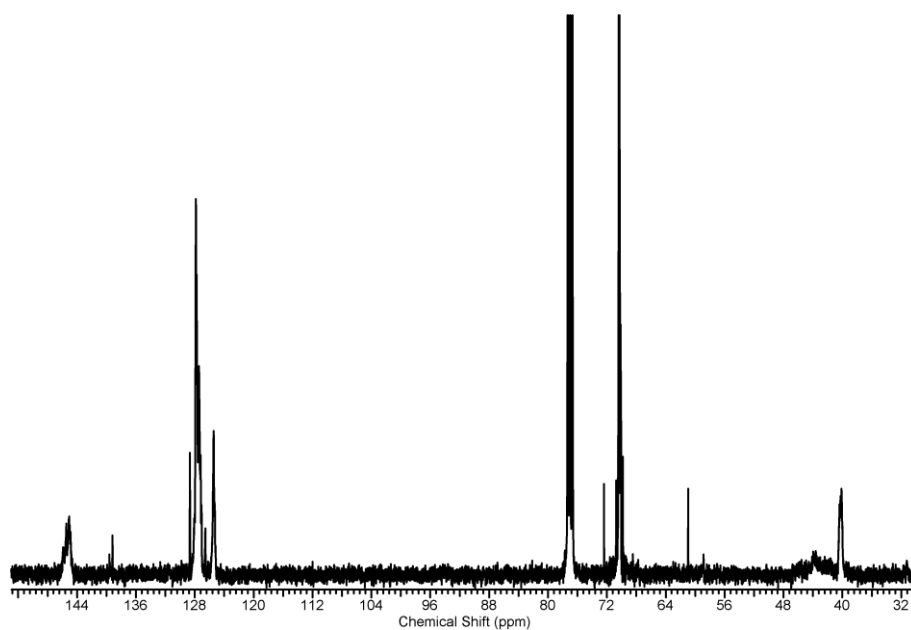


Fig. S 9: ^{13}C NMR spectrum of PS-DBAG-*b*-PEO (#10).

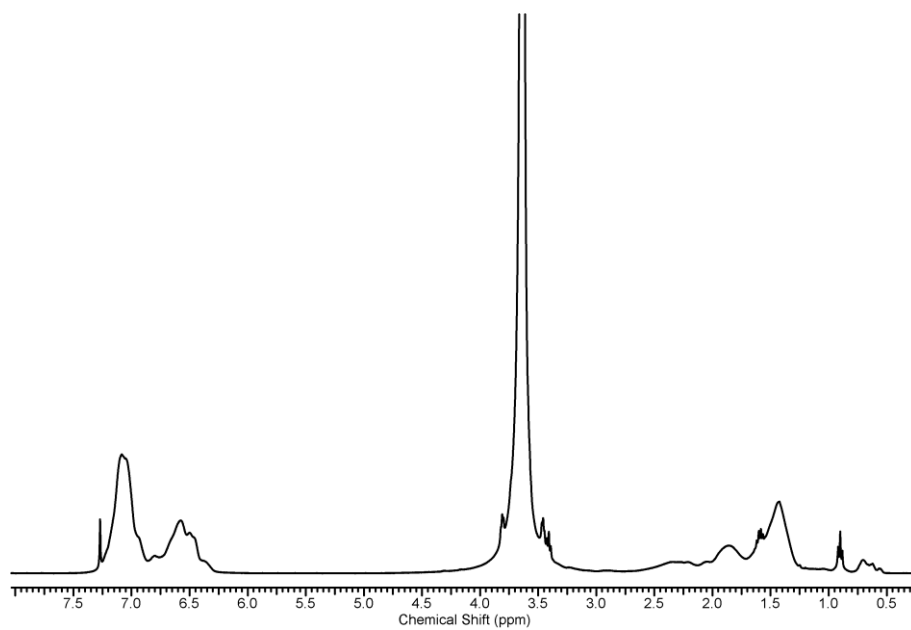


Fig. S 10: ^1H NMR spectrum of PS-(NH₂)-*b*-PEO (#17).

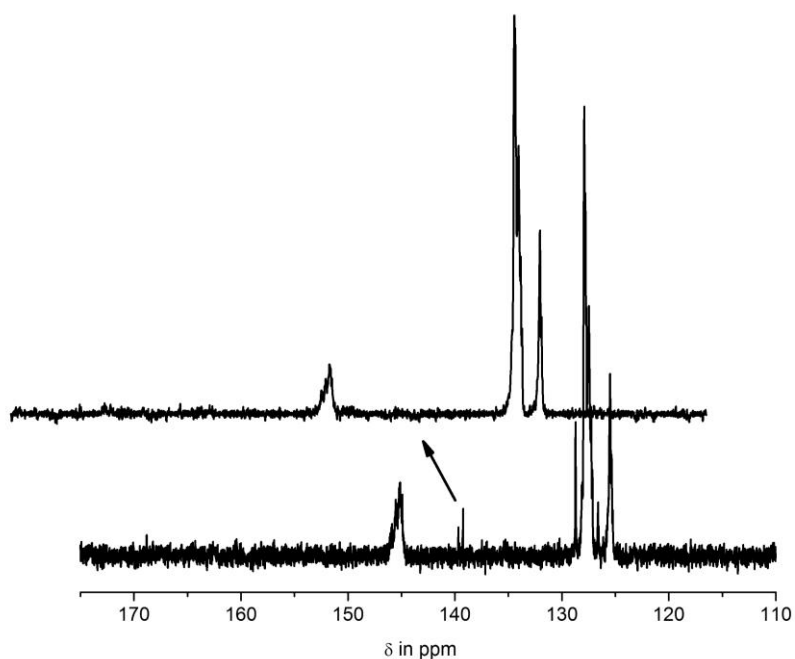


Fig. S 11: ^{13}C NMR spectrum of PS-(DBAG)-*b*-PEO (#14, bottom) and PS-(NH₂)-*b*-PEO (#17, top).

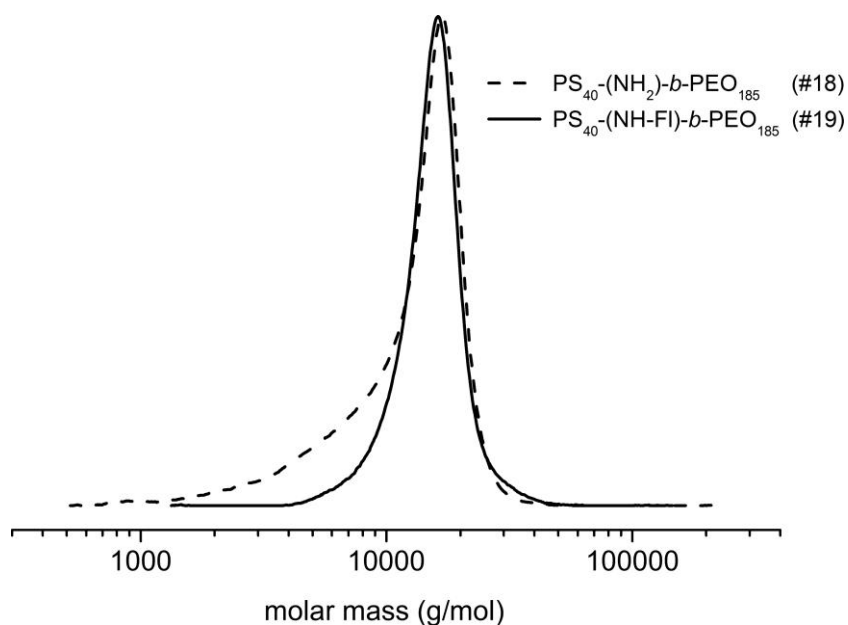


Fig. S 12: SEC traces of PS-(NH₂)-*b*-PEO (#18, dashed line) and PS-(NH-FI)-*b*-PEO (#19, solid line). The polydispersity of #19 is decreased compared to #18, which might be due to lower interaction between the column material and the fluorescent dye in comparison with the amino functionality.

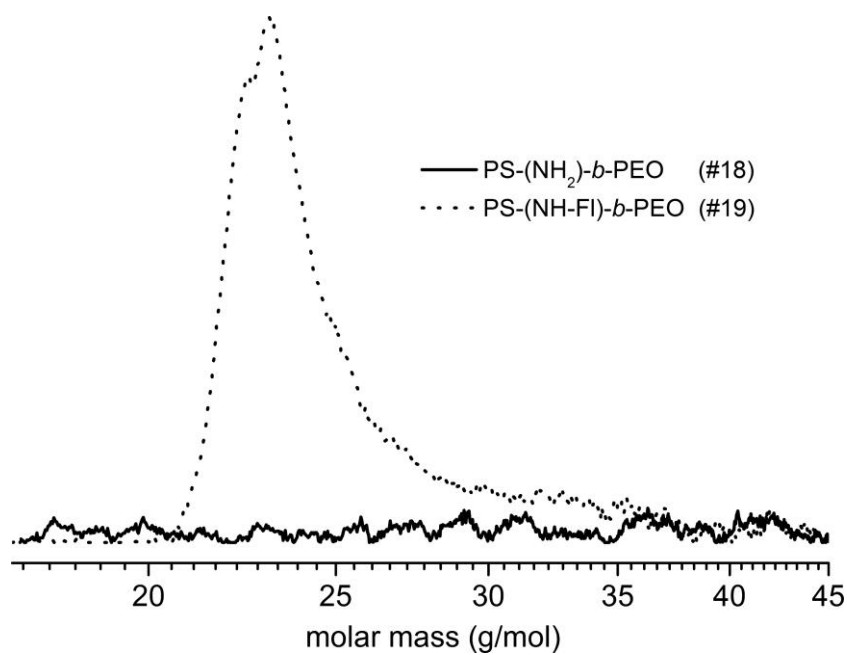


Fig. S 13: SEC traces of PS-(NH₂)-*b*-PEO (#18, solid line) and PS-(NH-FI)-*b*-PEO (#19, dotted line) with UV-signals at an absorption wavelength of 500 nm. The difference in signal strength (#19 strong signal, #18 no signal observable) indicating the successful incorporation of fluorescein at the block copolymer.

References

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