Supporting Information

Visible Light-Induced Iniferter Polymerization of Methacrylates Enhanced by Continuous Flow

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Content

Materials

The monomers n-butyl methacrylate (*n*BMA, Acros, 99%), methyl methacrylate (MMA, Acros, 99%), 2-ethyl metharcylate (EMA, Acros, 99%), 2-hydroxyethyl methacrylate (HEMA, Acros,99%) and diethyl glycol ether methacrylate (DEGMA, Acros, 99%) were deinhibited over a column of activated basic alumina, prior to use. 4-Cyano-4-[(dodecylsulfanylthiocarbonyl)sulfanyl]pentanoic acid (CDP-TTC) was synthesized according to literature.[1] The reagents and chemicals that were used for the synthesis of CDP-TTC were purchased from Sigma Aldrich or VWR. DMSO (Fisher, 99%) was used as received.

Characterization

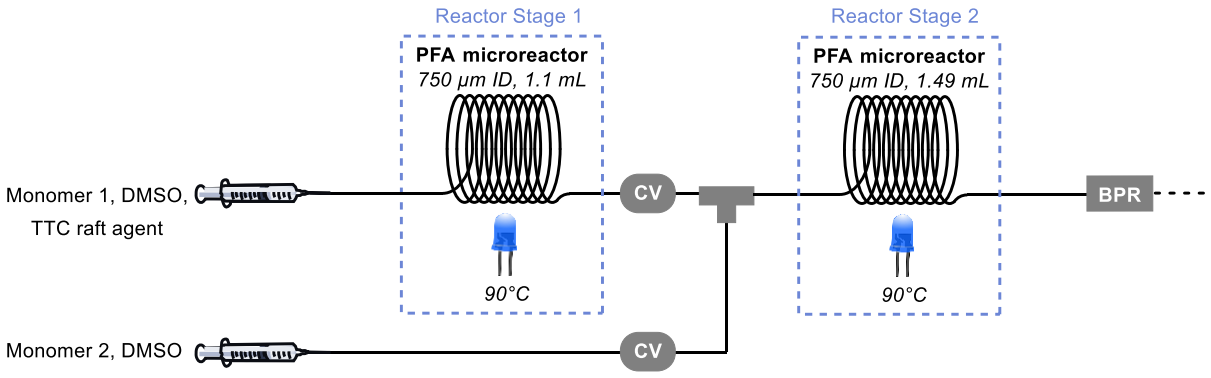
Monomer conversions were determined via Nuclear Magnetic Resonance spectra, which were recorded in $CDCl_3$ at room temperature on a Varian Inova spectrometer at 400 MHz for ^{1}H NMR using a 5 mm OneNMR PFG probe (Agilent Technologies Inc, Santa Clara, CA, USA). Free induction decays were collected with a 90° pulse of 6.9 μs, a spectral width of 6400 Hz, an acquisition time of 3 s, a preparation delay of 12 s and 64 accumulations.

Size-exclusion chromatography (SEC) was performed on a Tosoh EcoSEC HLC-8320GPC, operated by PSS WinGPC software, equipped with a PLgel 5.0 μm guard column (50 x 7.5 mm), followed by three PLgel 5 μm mixed-C columns (300 x 8 mm) and a differential refractive index detector using THF as eluent at 40°C with a flow rate of 1 mL min^{-1}. The SEC system was calibrated using linear narrow PS standards ranging from 474 – 7.5 x 10^6 g mol^{-1} (K = 14.1 x 10^{-5} dL g^{-1} and α = 0.70), and toluene as a flow marker. Molar masses and dispersity values were calculated against the Mark-Houwink parameters of the various monomers when available (PHEMA: K = 23.9 x 10^{-5} dL g^{-1} and α = 0.537,[1] PMMA: K = 9.44 x 10^{-5} dL g^{-1} and α = 0.719,[2] PBMA: K = 14.8 x 10^{-5} dL g^{-1} and α = 0.664,[2] PEMA: K = 9.7 x 10^{-5} dL g^{-1} and α = 0.714).[2] For block copolymers always the MHKS of the first polymer block were applied to approximate the true molecular weight as good as possible.

[1] R. Ferrari, Y. Yu, M. Morbidelli, R. A. Hutchinson and D. Moscatelli, *Macromolecules* 2011, **44**, 9205–9212.
[2] S. Beuermann, M. Buback, T. P. Davis, R. G. Gilbert, R. A. Hutchinson, A. Kajiwara, B. Klumperman and G. T. Russell, *Macromol. Chem. Phys.* 2000, **201**, 1355–1364.

Reactor design

As described in the experimental section, a self-made tubular reactor is designed for the photopolymerizations. Fluorinated gastight PFA tubing is wrapped around a glass framework and placed in a silicon oil bath with a temperature controlled to 90°C. Inside the glass framework 2 m of blue led strip is placed facing the PFA tubing. The reactor volumes are adjusted by varying the length of reactor tubing. Our initial studies focused upon the homopolymerization of methyl methacrylate and require a total internal reactor volume of 1.1 mL. Varying the flowrate results in varying residence times. The flowrate of the reaction mixture is controlled using a Fusion 100 classic syringe pump, and 10 mL SGE gastight syringes are used (Traja Scientific Australia, Pty Ltd.). Also, a reactor cascade is built consisting out of two reactor stages (1.1 mL + 1.49 mL) wrapped around the same glass framework and illuminated by the same light source (2m led strip, 120 LEDs, 450 nm 14.4 W/m). Efficient mixing between the viscous output stream of reactor stage 1 (1.1 mL) and the additional non-viscous monomer solution is ensured by a static micro mixing tee (U-466) and the use of check valves to eliminate backflow due to difference in flowrates and pressure drops.



Scheme S1. Schematic Representation of reactor cascade. CV = check valve, BPR = back pressure regulator

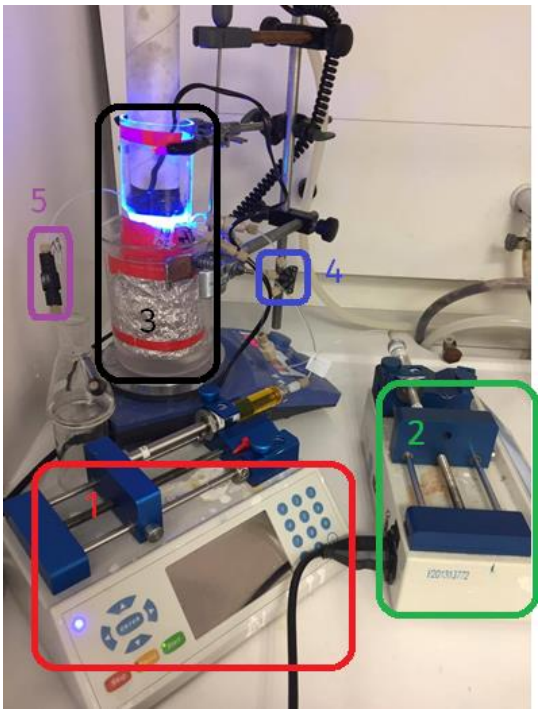


Figure S1. Setup of photoflow reactor. 1. Syringe pump reactor stage 1, 2. Syringe pump reactor stage 2, 3. Microreactor, 4. U-466 micro mixing tee and check valves, 5. Backpressure regulator 40 PSI.

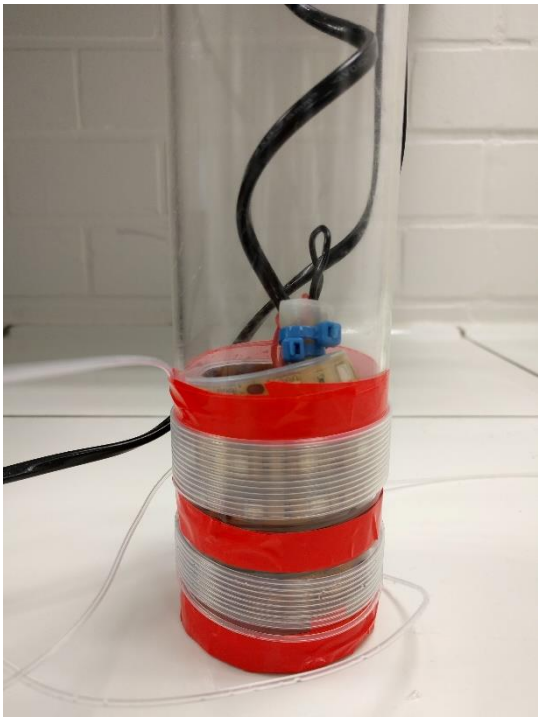


Figure S2. Closeup of both reactor stages. Reactor stage 1 (1.1 mL) is wrapped around the bottom part of the glass framework. Reactor stage 2 (1.49 mL) is wrapped around the top part of the glass framework. Reflective foil wrapped around outside glass framework is removed for clarity.

Continuous RAFT homopolymerization

In a typical procedure, 25 mmol (2.503 g, 50 equiv., 3.7 M) of the monomer MMA and 0.5 mmol (0.202g, 1 equiv.) of the RAFT agent CDP-TTC is dissolved in 6.80 ml of DMSO. The solution is kept in a sealed amber colored vial and subsequently is purged with nitrogen gas for 5 minutes. Next, the solution is transferred to one 10 ml gastight SGE syringe that is covered by aluminum foil. A 1.1mL tubular reactor is employed for the polymerization at a temperature of 90°C under illumination with blue light (450 nm) with a residence time of 60 min (0.0183 mL·min^{-1} flow rate). Monomer conversions are determined *via* ^{1}H NMR (>95%) (Figure S1). Molecular weight distributions are analyzed *via* SEC (2930 g·mol^{-1}, $Đ$ = 1.25). Identical procedures are also followed for the polymerization of EMA, *n*BMA, HEMA and DEGMA, by employing a monomer concentration of 3.7 M. Longer chain lengths could also be targeted by varying the MMA/CDP-TTC ratio through changing the raft agent concentration accordingly.

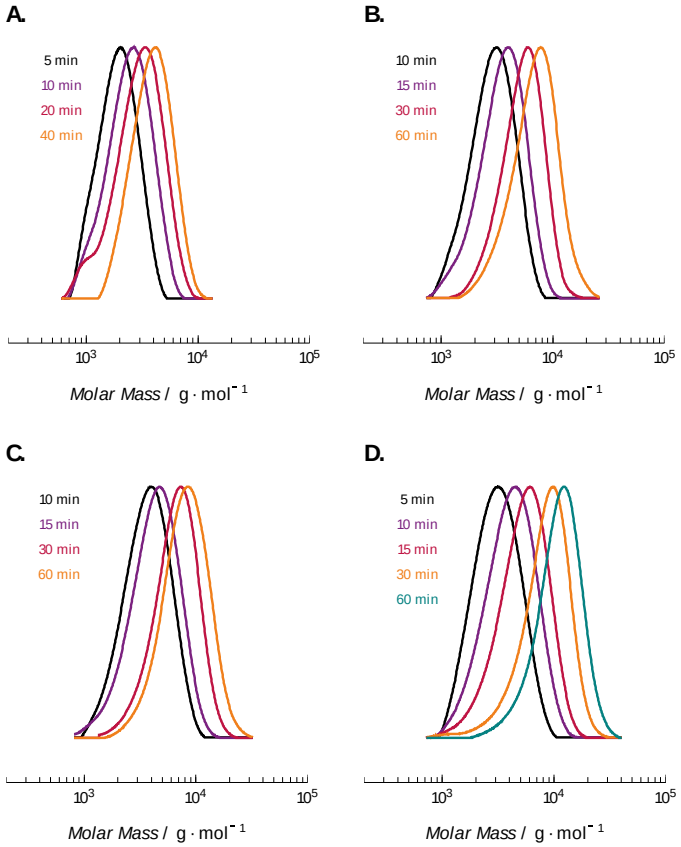


Figure S3. **A.** GPC traces of MMA 25 equiv. **B.** GPC traces of MMA 50 equiv. **C.** GPC traces of MMA 75 equiv. **D.** GPC traces of MMA 100 equiv.

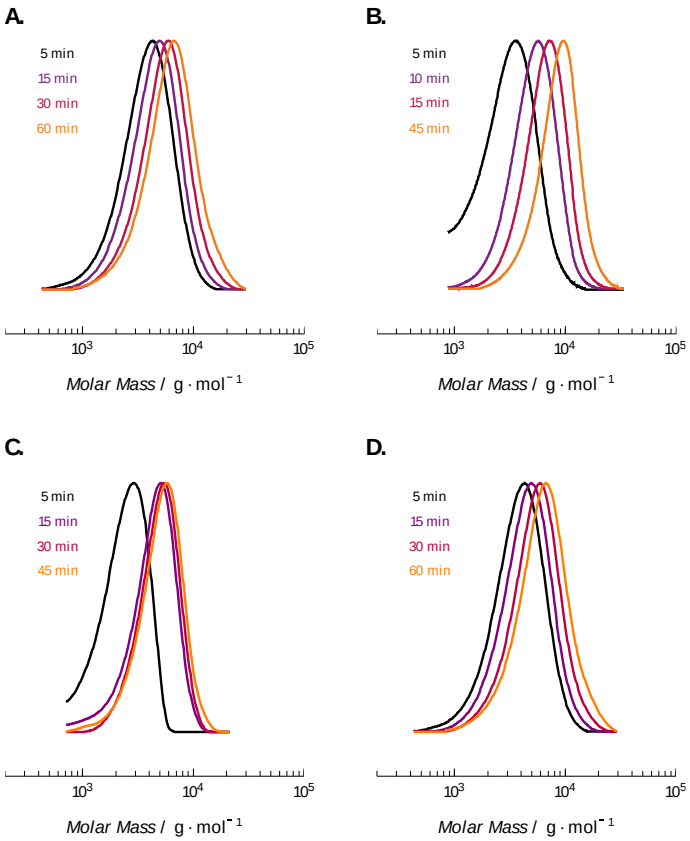


Figure S4. **A.** GPC traces of *p*EMA 50 equiv. **B.** GPC traces of *p*BMA 50 equiv. **C.** GPC traces of *p*HEMA 50 equiv. **D.** GPC traces of pDEGMA 50 equiv . Note that all chromatograms were obtained via THF-GPC

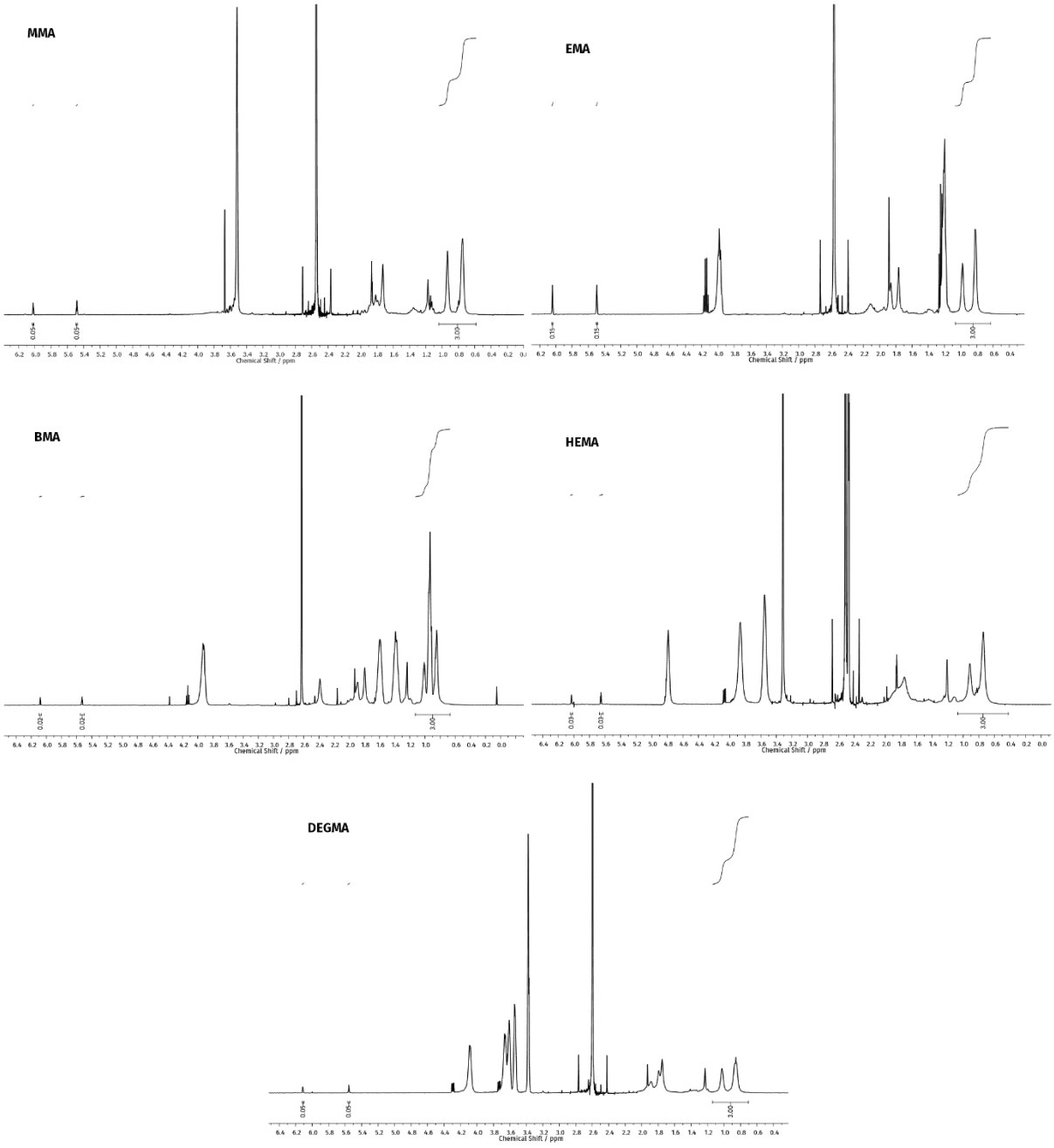


Figure S5. Determination of the monomer conversions of MMA, EMA, *n*BMA, HEMA and DEGMA homopolymers *via* ^{1}H NMR: comparing the average integration of the C**H$_2$**=C- peaks (monomer) to the integration of the -CH$_2$-C(C**H$_3$**)O- peak as reference integrated for three protons (polymer backbone). The average of the integrated (I_{CH_2}) monomer methylene peaks permits the calculation of the conversion with the formula: $monomer\ conversion = \frac{1}{1+(I_{CH_2})}$

Diblock copolymerizations by reinsertion in one continuous flow reactor

The first stock solution is prepared like the homopolymerizations resulting in *p*MMA (M_n = 2790 g·mol^{-1}, Đ = 1.23). 5 ml of this reaction mixture is collected, and without purification 18.4 mmol (1.842 g, 25 equiv., 3.3M) MMA and 0.55ml of DMSO is added. The solution is kept in a sealed amber colored vial and subsequently is purged with nitrogen gas for 5 minutes. Next, the solution is transferred to one 10 ml gastight SGE syringe that is covered by aluminum foil. The solution is inserted into the same 1.1 ml tubular reactor at 90°C and illuminated with blue light, for a total residence time of 60 minutes (0.0183 mL·min^{-1} flow rate). Monomer conversions of the second block are determined *via* ^{1}H NMR (>95%) and molecular weight distributions are analyzed *via* SEC (5170 g·mol^{-1}, *Đ* = 1.25). Similar strategies are followed to develop a large variety of diblock copolymers based on EMA, HEMA and DEGMA.

Table S1: Diblock copolymers based on *p*MMA as first block, obtained from a 1.1 tubular reactor reinsertion protocol without intermediate purification or isolation. The first block (homopolymer *p*MMA – entry 1) was carried out in the 1.1 mL reactor, with a monomer concentration of 3.7M, at 90°C and illuminated with blue light (450nm) for a 60 min residence time. The second block was directly polymerized in the same 1.1 mL reactor at 90°C and illuminated with blue light (450nm) with 60 min residence time.

Entry	*Polymer*	$[M]_0$ / M	*Conversion* / %	*Đ*	M_n^{app} / g · mol^{-1}	M_n^{theory} / g · mol^{-1}
1	*p*MMA	-	96	1.23	2790	2907
2	*p*MMA-*b*-*p*MMA	3.3	93	1.25	5170	5410
3	*p*MMA-*b*-*p*EMA	3.3	94	1.28	5450	5760
4	*p*MMA-*b*-*p*HEMA	3.3	98	1.27	5360	6160
5	*p*MMA-*b*-*p*DEGMA	3.3	98	1.33	7230	7610

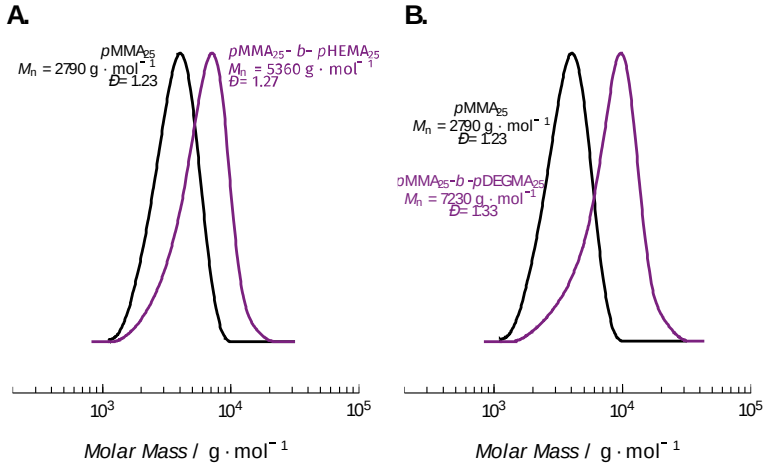


Figure S6: **A.** *p*MMA-*b*-*p*HEMA GPC trace. **B.** *p*MMA-*b*-*p*DEGMA GPC trace.

Triblock copolymerizations by reinsertion in one continuous flow reactor

The diblock copolymer *p*MMA-*b*-*p*EMA (5450g·mol^{-1}, *Đ* = 1.28) os prepared as described in the previous section. 3.5 ml of this reaction mixture is collected, and without intermediate purification 12.88 mmol (1.289g, 25equiv., 3.31M) MMA and 0.39ml of DMSO is added. The solution is kept in a sealed amber colored vial and subsequently is purged with nitrogen gas for 5 minutes. Next, the solution is transferred to one 10 ml gastight SGE syringe covered by aluminum foil. The solution is inserted into the same 1.1 ml tubular reactor at 90°C and illuminated with blue light, for a total residence time of 60 minutes (0.0183 mL·min^{-1} flow rate). Monomer conversions of the second block are determined *via* ^{1}H NMR (>95%) and molecular weight distributions are analyzed *via* SEC (7920 g·mol^{-1}, *Đ* = 1.32).

Table S2: Triblock copolymers based on *p*MMA-*b*-*p*EMA as first diblock copolymer, obtained from a 1.1 tubular reactor reinsertion protocol without intermediate purification or isolation. The first diblock (*p*MMA-*b*-*p*EMA – entry 1) was carried out in the 1.1 mL reactor, with a monomer concentration of 3.3M, at 90°C and illuminated with blue light (450nm) for a 60 min residence time. The second block was directly polymerized in the same 1.1 mL reactor at 90°C and illuminated with blue light (450nm) with 60 min residence time.

Entry	*Polymer*	$[M]_0$ / M	*Conversion* / %	*Đ*	M_n^{app} / g · mol^{-1}	M_n^{theory} / g · mol^{-1}
1	*p*MMA-*b*-*p*EMA	-	94	1.28	5450	5760
2	*p*MMA-*b*-*p*EMA-*b*-*p*MMA	3.3	90	1.32	7920	8260

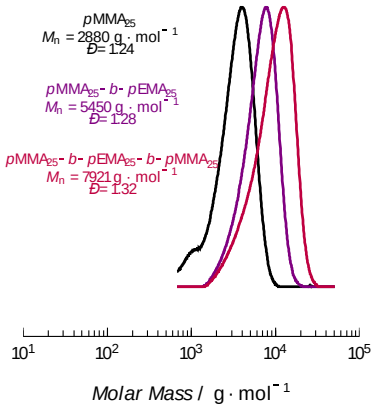


Figure S7: *p*MMA-*b*-*p*EMA-*b*-*p*MMA GPC trace

Diblock copolymerizations by continuous flow reactor cascade

The first stock solution is prepared like the homopolymerizations resulting in *p*MMA (M_n = 2930 g·mol^{-1}, Đ = 1.25). In a second stock solution, 18.4 mmol (1.842 g, 25 equiv., 3.3M) MMA is dissolved in 0.55ml of DMSO. The solution is kept in a sealed amber colored vial and subsequently is purged with nitrogen gas for 5 minutes. Next, the solution is transferred to one 10 ml gastight SGE syringe that is covered by aluminum foil. A [1.1 mL + 1.49 mL] tubular reactor cascade is employed for the polymerizations. The residence time for the first block is kept constant at 60min (0.0183 mL·min^{-1} flow rate reactor 1), while also 60 min residence time is employed for the second block (0.0248 mL·min^{-1} total flow rate reactor 2). Thus, the second stock solution is pumped with a flowrate of 0.0065 mL·min^{-1}. Monomer conversions of the second block are determined *via* ^{1}H NMR (96%) and molecular weight distributions are analyzed *via* SEC (5250 g mol^{-1}, *Đ* = 1.28). Similar strategies are followed to develop a large variety of diblock copolymers based on five different methacrylates; MMA, EMA, *n*BMA, HEMA and DEGMA.

Table S3: Diblock copolymers based on *p*MMA or *p*HEMA as first block, obtained from a [1.1 mL + 1.49 mL] tubular reactor cascade without intermediate purification or isolation. The first block (homopolymer *p*MMA, – entry 1, *p*HEMA – entry 7) was carried out in the first 1.1 mL reactor, with a monomer concentration of 3.7M, at 90°C and illuminated with blue light (450nm) for a 60 min residence time. The second block was carried out in the second 1.49 mL reactor at 90°C and illuminated with blue light (450nm) with a 60 min residence time.

Entry	*Polymer*	$[M]_0$ / M	*Conversion* / %	*Đ*	M_n^{app} / g · mol^{-1}	M_n^{theory} / g · mol^{-1}
1	*p*MMA	-	96	1.25	2930	2910
2	*p*MMA-*b*-*p*MMA	3.3	96	1.28	5250	5410
3	*p*MMA-*b*-*p*EMA	3.3	92	1.32	5280	5760
4	*p*MMA-*b*-*p*BMA	3.3	99	1.30	5870	6460
5	*p*MMA-*b*-*p*HEMA	3.3	98	1.30	5770	6160
6	*p*MMA-*b*-*p*DEGMA	3.3	98	1.27	5900	7610
7	*p*HEMA	-	97	1.25	3990	3650
8	*p*HEMA-*b*-*p*HEMA	3.3	96	1.30	7280	6900
9	*p*HEMA-*b*-*p*MMA	3.3	93	1.27	6510	6150
10	*p*HEMA-*b*-*p*BMA	3.3	98	1.30	8760	7200
11	*p*HEMA-*b*-*p*DEGMA	3.3	96	1.29	8390	8360

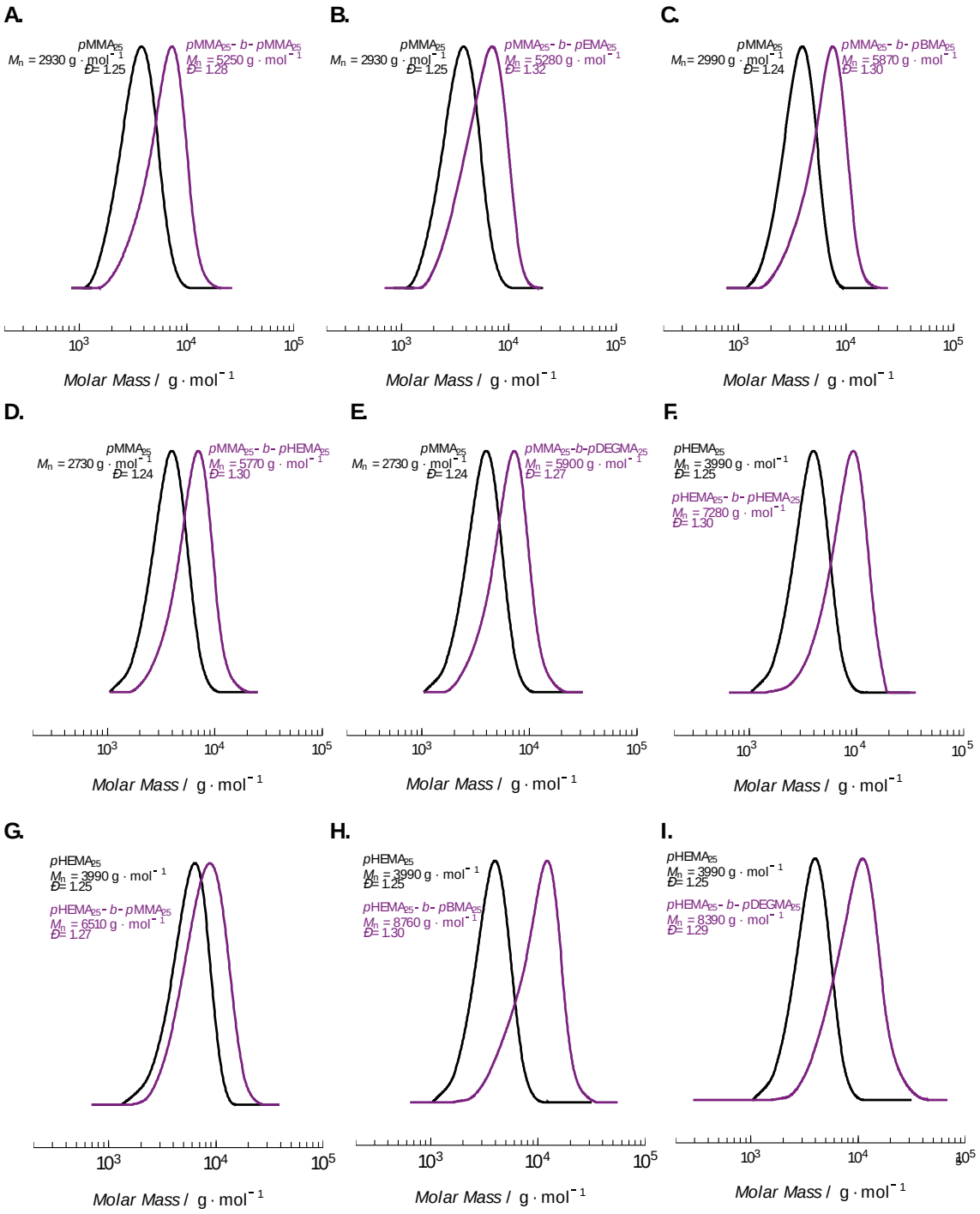


Figure S8: **A.** *p*MMA-*b*-*p*MMA GPC trace. **B.** *p*MMA-*b*-*p*EMA GPC trace. **C.** *p*MMA-*b*-*p*BMA GPC trace. **D.** *p*MMA-*b*-*p*HEMA GPC trace. **E.** *p*MMA-*b*-*p*DEGMA GPC trace. **F.** *p*HEMA-*b*-*p*HEMA GPC trace. **G.** *p*HEMA-*b*-*p*MMA GPC trace. **H.** *p*HEMA-*b*-*p*BMA GPC trace. **I.** *p*HEMA-*b*-*p*DEGMA GPC trace.

1. Kang, H.U., et al., *One-step synthesis of block copolymers using a hydroxyl-functionalized trithiocarbonate RAFT agent as a dual initiator for RAFT polymerization and ROP.* Journal of Polymer Science Part A: Polymer Chemistry, 2013. **51**(4): p. 774-779.