

Supporting Information

Continuous Flow Synthesis of Core Cross-Linked Star Polymers *via* Photo-Induced Copper Mediated Polymerization

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Content

Materials.....	S 2
Core cross-linked star polymer synthesis in batch.....	S 2
Characterization	S 3
Reactor design	S 6
SEC evolution of CCS polymer formation <i>via</i> flow and batch polymerization.....	S 7
Surface functionalized core cross-linked star polymer synthesis in a reactor cascade	S 8
Pseudomiktoarm core cross-linked star polymer synthesis in a flow reactor cascade.....	S 9
References.....	S 10

Materials

The monomers methyl acrylate (MA, Acros Organics, 99%) and benzyl acrylate (BnA, TCI Chemicals, >97%) and the crosslinker 1,4-butanediol diacrylate (BDDA, Sigma-Aldrich, 90%) were deinhibited over a column of activated basic alumina before polymerization. The initiator ethyl α -bromoisobutyrate (EBiB, 98%) and catalyst copper(II)dibromide ($\text{Cu}^{\text{II}}\text{Br}_2$, 99%) and radical inhibitor hydroquinone (HQ, 99%) were purchased from Acros Organics and used without further purification. The initiator 2-hydroxyethyl 2-bromoisobutyrate (HEBiB)¹ and the ligand tris-(2(dimethylamino)ethyl)amine (Me_6TREN)² were synthesized following literature procedures, the used chemicals for the synthesis were purchased from Fisher Scientific and Alfa Aesar. Dimethylsulfoxide (DMSO, pa grade), tetrahydrofuran (THF, HPLC grade), Chloroform (>99%) and N,N-dimethylformamide (DMF, 99%) were purchased from Fisher Scientific and used as received.

Core cross-linked star polymer synthesis in batch

A 10 mL solution of pMA ($M_n = 2600 \text{ g}\cdot\text{mol}^{-1}$, $D = 1.13$), $\text{Cu}^{\text{II}}\text{Br}_2$ and Me_6TREN in DMSO was prepared. A second 10 mL solution of BDDA and DMF in DMSO was made in a separate amber volumetric flask. (pMA : $\text{Cu}^{\text{II}}\text{Br}_2$: Me_6TREN : BDDA : DMF = 1 : 0.02 : 0.09 : 10 : 1; [pMA] = 0.0325 M). DMF was used as internal standard for determination of the cross-linker conversion via ^1H NMR. These were mixed together in an Erlenmeyer flask and purged with N_2 for 15 minutes before being placed in a Multilamp Reactor MLU 18 (Photochemical Reactor Ltd.) equipped with ten 15 W lamps (Vilber Lourmat) with a peak emission of 365 nm. Samples for SEC(-MALS) and ^1H -NMR were taken at timed intervals (5, 10, 15, 30 and 60 min). All samples for SEC(-MALS) were immediately quenched by diluting in THF, passing over a short silica column to remove the copper catalyst and addition of HQ.

Characterization

¹H NMR Monomer and crosslinker conversions were determined via Nuclear Magnetic Resonance spectra, which were recorded in CDCl₃ at room temperature on a Varian Inova spectrometer at 400 MHz for ¹H 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.

SEC(-MALS) Polymer size distributions were measured using a Tosoh EcoSEC HLC-8320GPC consisting out of an autosampler and a PSS guard column SDV (50 × 7.5 mm), followed by three PSS SDV analytical linear XL columns (5 μm, 300 × 7.5 mm) and a differential refractive index detector (Tosoh EcoSEC RI). Column temperature was maintained at a constant 40°C. A flow rate of 1·mL·min⁻¹ of high-performance liquid chromatography (HPLC) grade tetrahydrofuran (THF) was used as eluent with toluene as flow marker. Calibration was performed using linear narrow polystyrene (PS) standards from PSS Laboratories in the range of 470-7.5 × 10⁶ g·mol⁻¹. Mark-Houwink-Kuhn-Sakurada parameters for pMA ($\alpha = 0.74$, $K = 10.2 \times 10^{-5} \text{ dL}\cdot\text{g}^{-1}$, THF 30°C)³ were used for sample analysis. When SEC-MALS was performed a similar SEC setup connected to a Wyatt Optilab TrEX RI detector and a Wyatt Heleos Dawn II multiangular light scattering was used. The weight average molecular weight of the synthesized core cross-linked star polymers was determined via Astra V. More information regarding the used dn/dc values can be found below.

ESI-MS Spectral mass analysis was performed using an LCQ Fleet mass spectrometer (ThermoFischer Scientific) equipped with an atmospheric pressure ionization source set in nebulizer assisted electro spray mode. Calibration was performed in the mass/charge (m/z) range of 220–2000 with a standard solution containing caffeine, L-methionyl-arginyl-phenylalanylalanine acetate H₂O and Ultramark 1621. A constant spray voltage of 5 kV was employed with an applied nitrogen dimensionless auxiliary gas flow-rate of 3 and a dimensionless sheath gas flow-rate of 3. The capillary voltage, tube lens offset voltage and capillary temperature were set to 25, 120 V, and 275 °C, respectively. A 250 μL aliquot of

a polymer solution with concentration of $10 \mu\text{g}\cdot\text{mL}^{-1}$ was injected with HPLC grade THF and methanol (THF:methanol 3:2) as solvent.

Determination of arm number The arm number was determined via light scattering and following equations from literature^{4, 5}:

$$\frac{A_{star}}{A_{MI}} = \frac{A_{star}}{1 - A_{star}} = \frac{\left(\frac{dn}{dc}\right)_{star}(X_{MI}m_{MI} + m_{CL}conv_{CL})}{\left(\frac{dn}{dc}\right)_{MI}(1 - X_{MI})m_{MI}}$$

$$\left(\frac{dn}{dc}\right)_{star} = \frac{X_{MI}m_{MI}\left(\frac{dn}{dc}\right)_{MI} + m_{CL}conv_{CL}\left(\frac{dn}{dc}\right)_{CL}}{X_{MI}m_{MI} + m_{CL}conv_{CL}}$$

A_{star} and A_{MI} respectively are the integrated areas of the peaks that correspond to the star product and any residual MI from the differential refractive index SEC chromatograms. These areas are determined via peak analysis in Origin. The dn/dc value for linear pMA was reported in literature to have a value of $0.068 \text{ mL}\cdot\text{g}^{-1}$.⁶ The dn/dc value for linear pBnA was measured with an Optilab TrEX from Wyatt using the 100% mass recovery method and determined to be 0.112 in Astra V. The dn/dc value of the crosslinker was assumed to be similar to linear pMA $0.068 \text{ mL}\cdot\text{g}^{-1}$. The total mass of MI and crosslinker respectively are the values of m_{MI} and m_{CL} and are expressed in grams. The conversion of the crosslinker was determined with ¹H-NMR using DMF as internal standard. X_{MI} is the weight fraction of incorporated MIs and corrects for the fact that the measured M_w via light scattering is not only stemming from the incorporated arms, but also the cross-linker core. X_{MI} can be calculated as follows:

$$X_{MI} = \frac{A_{star}m_{MI}\left(\frac{dn}{dc}\right)_{MI} - (1 - A_{star})m_{CL}conv_{CL}\left(\frac{dn}{dc}\right)_{CL}}{m_{MI}\left(\frac{dn}{dc}\right)_{MI}}$$

After obtaining all these values the number average value of arms per star can now be calculated according to the following equation:

$$N_{arms} = \frac{M_{w, MALS}}{M_{n, MI}} \cdot \frac{X_{MI}m_{MI}}{X_{MI}m_{MI} + m_{CL}conv_{CL}}$$

$M_{w, \text{MALS}}$ is the weight-averaged molecular weight determined via MALS using Astra V from Wyatt Technologies. $M_{n, \text{MI}}$ is the number-averaged molecular weight of the MI obtained from SEC.

In case miktoarm core cross-linked star polymers were synthesized, the following formulas were employed to determine the average $(dn/dc)_{\text{MI}}$ value and $M_{n, \text{MI}}$:

$$\left(\frac{dn}{dc}\right)_{\text{MI}} = \frac{m_{\text{MI}-1} \left(\frac{dn}{dc}\right)_{\text{MI}-1} + m_{\text{MI}-2} \left(\frac{dn}{dc}\right)_{\text{MI}-2}}{m_{\text{MI}-1} + m_{\text{MI}-2}}$$

$$M_{n, \text{MI}} = M_{n, \text{MI},1} n_1 + M_{n, \text{MI},2} n_2$$

In which n_1 and n_2 the molar contributions are of respectively MI_1 and MI_2 as determined by ^1H NMR.

Reactor design

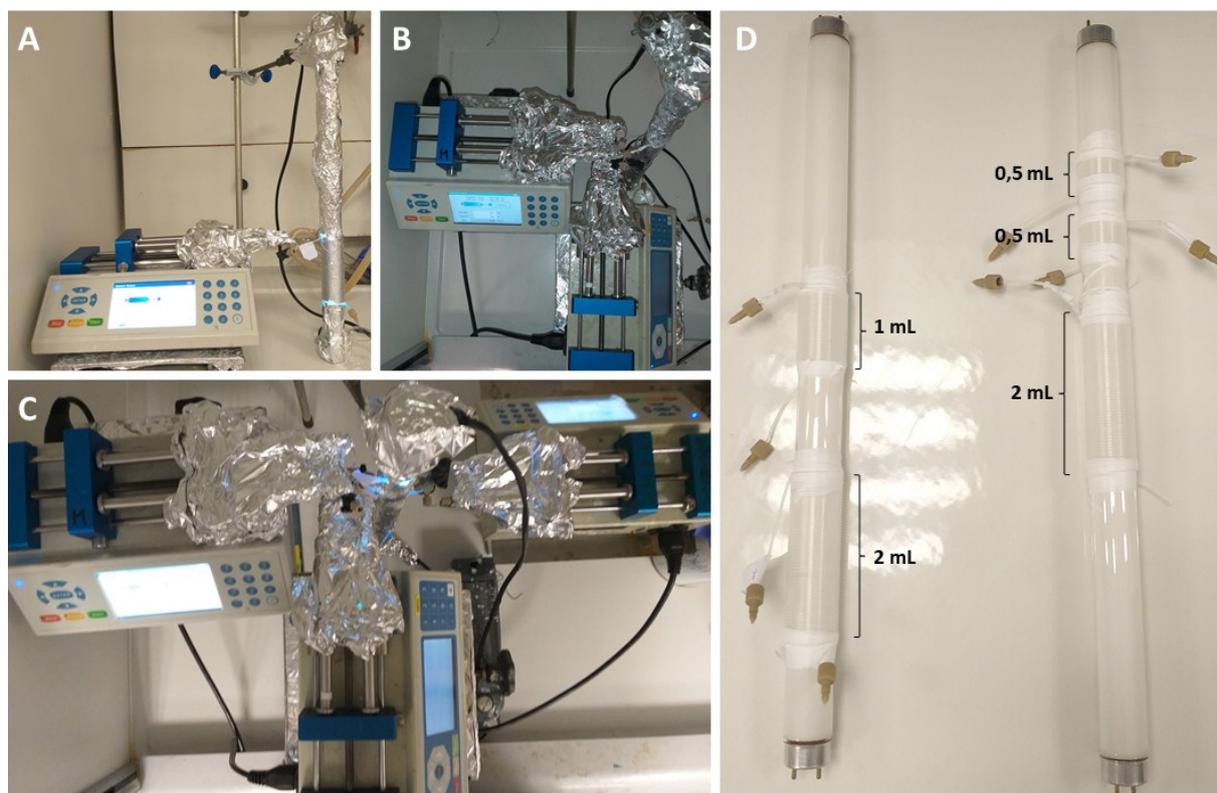


Fig. S1 Photos of the used reactors in the current work. A, 2 mL PFA flow reactor for core cross-linked star (CCS) polymer synthesis. B, reactor cascade composed of a 1 mL PFA flow reactor for macroinitiator (MI) synthesis connected to a 2 mL PFA flow reactor for CCS polymer synthesis (top view). C, Reactor cascade composed of 2 0.5 mL PFA flow reactors for MI synthesis connected to a 2 mL PFA flow reactor for mikroarm CCS polymer synthesis (top view). D, picture of the PFA flow tubing wrapped around the UV lamps.

SEC evolution of CCS polymer formation *via* flow and batch polymerization

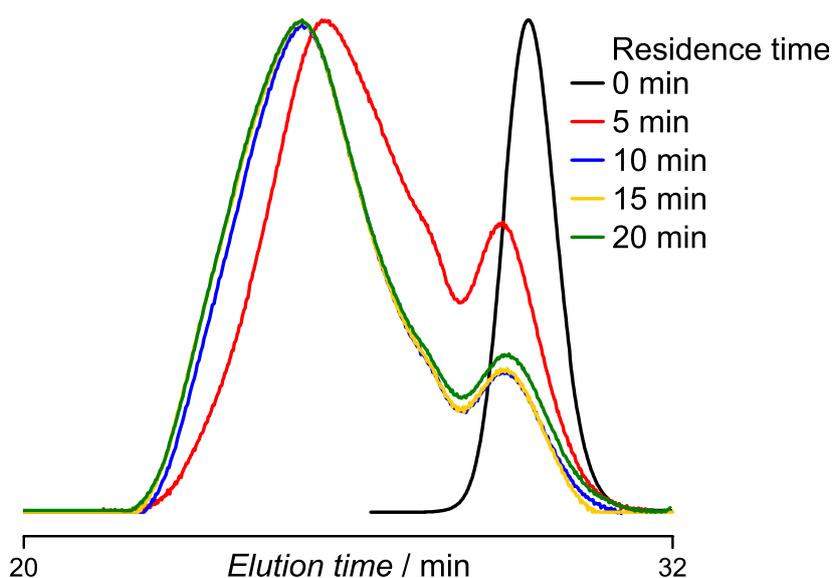


Fig. S2 Evolution of SEC elugrams for core cross-linked star polymer synthesis in flow at different residence times. A reaction ratio of pMA : Cu^{II}Br₂ : Me₆TREN : BDDA = 1 : 0.02 : 0.09 : 10 and [pMA] = 0.0325M was used. The pMA macroinitiator had an M_n of 2700 g·mol⁻¹.

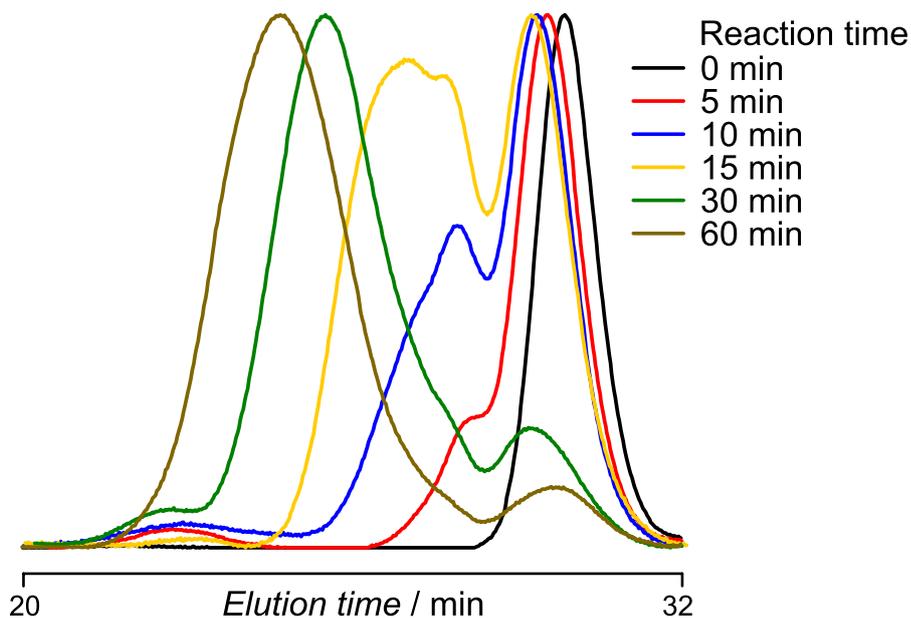


Fig. S3 Evolution of SEC elugrams for core cross-linked star polymer synthesis in batch at different reaction times. A reaction ratio of pMA : Cu^{II}Br₂ : Me₆TREN : BDDA = 1 : 0.02 : 0.09 : 10 and [pMA] = 0.0325M was used. The pMA macroinitiator had an M_n of 2600 g·mol⁻¹.

Surface functionalized core cross-linked star polymer synthesis in a flow reactor cascade

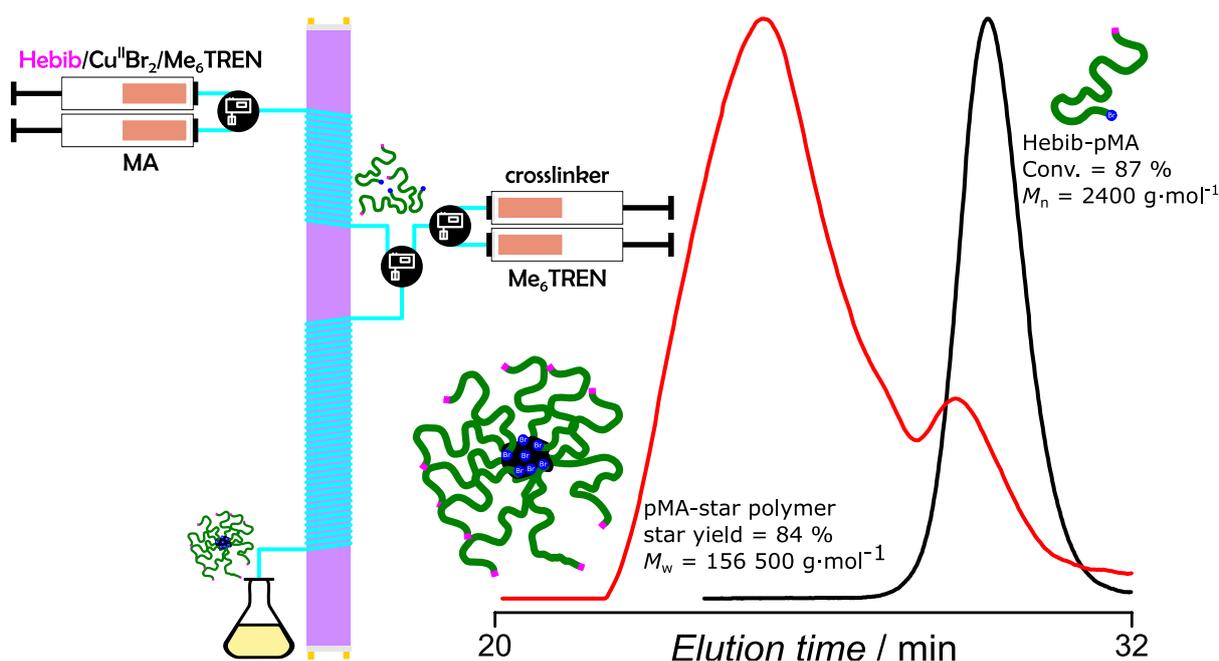
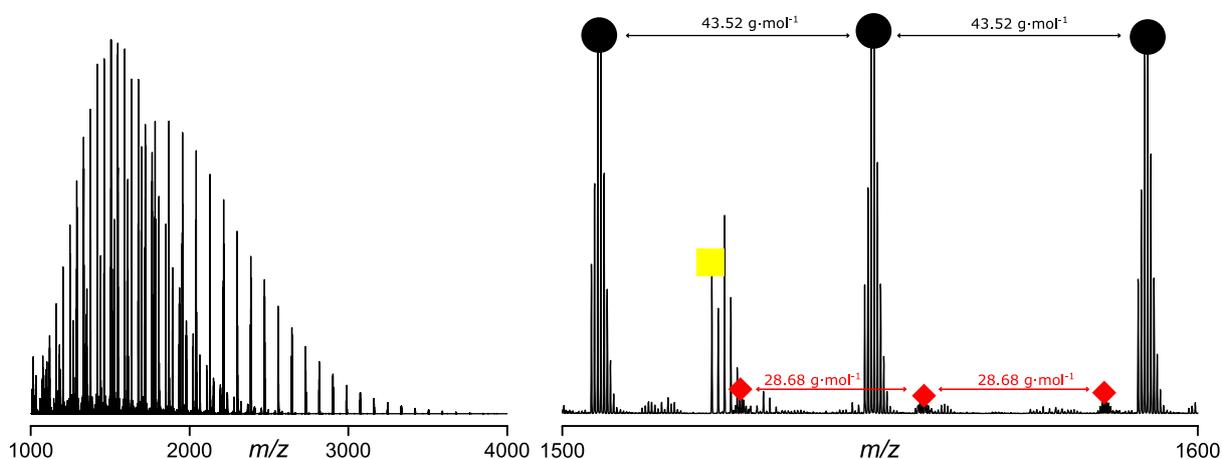


Fig. S4 Surface functionalized core cross-linked star (CCS) polymer synthesis in a reactor cascade. Left, schematic visualization of the reactor. Right, SEC elugram of the MI and resulting CCS polymer. Monomer conversion, star yield, $M_{n, MI}$ and $M_{w, CCS \text{ polymer}}$ are also given. A reaction ratio of $HEBiB:MA : Cu^{II}Br_2 : Me_6TREN : BDDA = 1 : 40 : 0.02 : 0.09 : 10$ corresponding to a targeted $[pMA] = 0.0325M$.



α end group	ω end group	end	Units MA	ion	$m/z_{exp.}$	m/z_{theo}
Hebib	Br	15		Na^+	1523.53	1523.53
Hebib	Br	32		$2 Na^+$	1504.57	1504.57
Hebib	Br	33		$2 Na^+$	1547.59	1547.59
Hebib	Br	34		$2 Na^+$	1590.61	1590.61
Hebib	Br	50		$3 Na^+$	1526.93	1526.93
Hebib	Br	51		$3 Na^+$	1555.95	1555.61
Hebib	Br	52		$3 Na^+$	1584.29	1584.29

Fig. S5 Electrospray ionization mass spectrometry measurement on the arms synthesized using HEBiB as initiator. Top left, complete mass spectrum. Top right, zoomed mass spectrum. Bottom table, assignment of the observed peaks in the top right spectrum.

Pseudomiktoarm core cross-linked star polymer synthesis in a flow reactor cascade

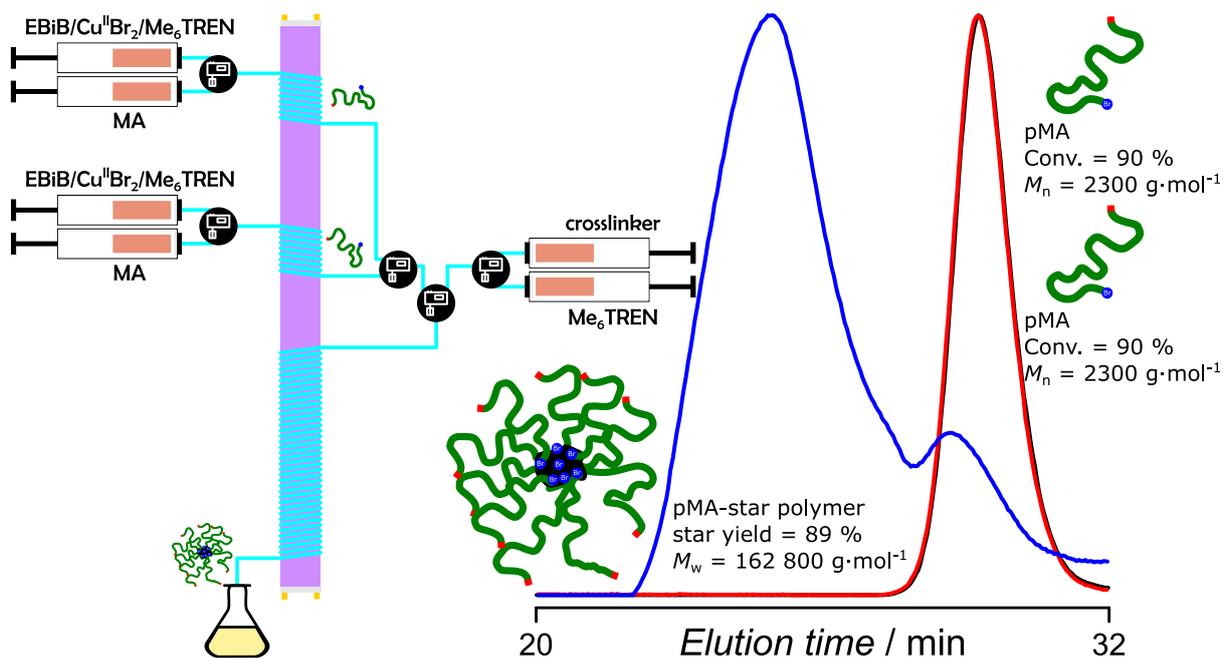


Fig. S6 Pseudomiktoarm core cross-linked star (CCS) polymer synthesis in a reactor cascade. Left, schematic visualization of the reactor. Right, SEC elugram of the MIs and resulting CCS polymer. Monomer conversion, star yield, M_n , M_w and M_w , CCS polymer are also given. A reaction ratio of EBiB : MA : Cu^{II}Br₂ : Me₆TREN : BDDA = 1 : 40 : 0.02 : 0.09 : 10 corresponding to a targeted [MI] = 0.0325M.

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