Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

RAFT Multiblock Reactor Telescoping: From Monomers to Tetrablock Copolymers in a Continuous Multistage Reactor Cascade

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Content

Materials

n-Butyl acrylate (*n*BuA) (Acros, 99%), methyl acrylate (MA) (Acros, 99%), ethyl acrylate (EA) (Acros, 99.5%), *t*-butyl acrylate (*t*BuA) (J&K, 98.5%), 2-hydroxyethyl acrylate (HEA) (TCI, 95%), *N*-isopropylacrylamide (NIPAM) (Acros, 99%), 2-ethylhexyl acrylate (EHA) (TCI, 99%) and 2-(2-ethoxyethoxy)ethyl acrylate (DEGA) (TCI, 98%) were deinhibited over a column of activated basic alumina, prior to use. 1,1'-azobis(isobutyronitrile) (AIBN) (Sigma-Aldrich, 98%) was recrystallized twice from methanol prior to use. 2-(dodecylthiocarbonothioylthio)propionic acid (DoPAT)) was synthesized according to a literature procedure.[1] *n*-Butanol (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 ^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. A line-broadening factor of 0.2 Hz was applied before Fourier transformation to the frequency domain. In order to determine monomer conversion of the last block in tri- and tetrablock copolymers, dibromomethane was added to the stock solution and employed as internal standard.

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 PnBuA (K = 12.2 x 10^{-5} dL g^{-1} and α = 0.70).

In-Situ FT-IR spectroscopy was employed to monitor monomer conversions by measuring the area of the acrylate peaks (1650 – 1605 cm^{-1}). Therefore, a ReactIR 15 (Mettler Toledo) spectrometer, equipped with a DS Micro Flow Cell with an optical range 4000 – 650 cm^{-1} was connected to the employed reactor set-up.

ESI-MS was performed using a LTQ orbitrap velos pro mass spectrometer (ThermoFisher Scientific) equipped with an atmospheric pressure ionization source operating in the nebulizer assisted electrospray mode. The instrument was calibrated in the m/z range 220 – 200 using a LTQ Velos ESI Positive Ion Calibration Solution. A constant spray voltage of 5 kV was used. Capillary temperature was set to 275°C. A mixture of THF and methanol (3/2, HPLC grade) was used as solvent. Spectra were analyzed in Thermo Xcalibur Qual Browser software.

Continuous RAFT homopolymerization

In a typical procedure, 40 mmol (5.127 g, 10 equiv., 4 M) of the monomer *n*BuA, 4 mmol (1.402 g, 1 equiv.) of the RAFT agent DoPAT and 0.2 mmol (33 mg, 0.05 equiv.) of the initiator AIBN were dissolved in *n*-butanol. The solution was kept in a sealed Duran flask, connected to the reactor set-up *via* a HPLC pump and purged with Ar prior to use. A 0.8 mL tubular reactor was employed for the polymerization at a temperature of 100°C with a residence time of 16 min (0.050 mL min^{-1} flow rate). Monomer conversions were determined *via* ^{1}H NMR (95%) (Figure S1). Molecular weight distributions were analyzed *via* SEC (1630 g mol^{-1}, $Đ$ = 1.11). Identical procedures were also followed for the polymerization of MA, EA, *t*BuA and HEA, by employing a monomer concentration of 4 M, while lower monomer concentrations were employed for EHA (2.7 M) and DEGA (3 M). Long chain lengths could also be targeted by varying the *n*BuA/DoPAT ratio, keeping the monomer concentration constant at 4 M (except of the DP 5 polymer where a 2 M *n*BuA concentration was employed) (Figure 5).

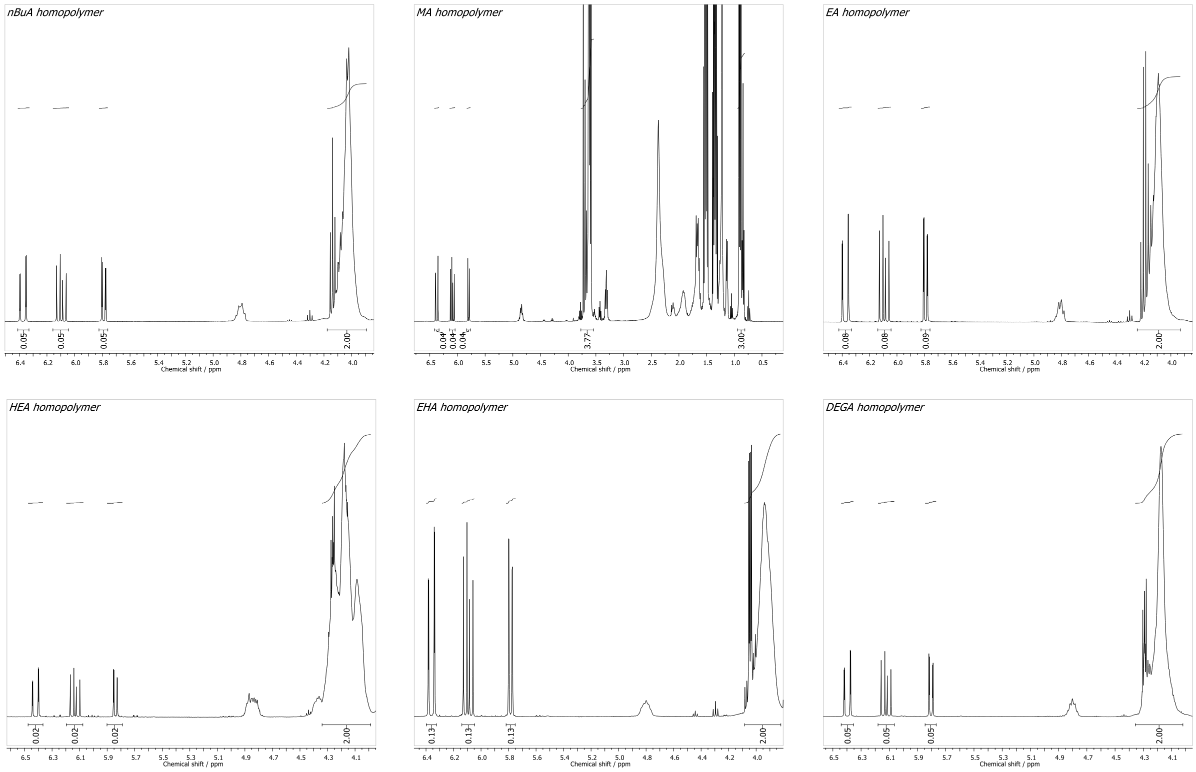


Figure S1. Determination of the monomer conversions of *n*BuA, MA, EA, HEA, EHA and DEGA homopolymers *via* ^{1}H NMR: comparing the average integration of the C**H**$_2$=C**H**- peaks (monomer) to the integration of the -C**H**$_2$-CO peak (monomer + polymer side chain). (Except for MA, where the overlapping solvent peak was taken into account as well.)

Continuous diblock copolymerizations

The first stock solution was prepared similar to the homopolymerizations. In a second stock solution, 50 mmol (4.305 g, 10 equiv., 5 M) MA and 0.25 mmol (41 mg, 0.05 equiv.) AIBN were dissolved in *n*-butanol. The solution was kept in a sealed Duran flask at 0°C and protected from light. The solution was connected to the reactor set-up *via* a second HPLC pump and purged with Ar prior to use. A [0.8 mL + 3.6 mL] tubular reactor cascade was employed for the polymerizations. The residence time for the first block was kept constant at 16 min (0.050 mL min^{-1} flow rate 1), while 40 min residence time was employed for the second block (0.040 mL min^{-1} flow rate 2). Monomer conversions of the second block were determined *via* ^{1}H NMR (96%) and molecular weight distributions were analyzed *via* SEC (1950 g mol^{-1}, $Đ$ = 1.21). Similar strategies were followed to develop a large variety of diblock copolymers based on 7 different acrylates and an acrylamide. Depending on the monomer concentrations, flow rates could be adjusted to assure a 1/1 monomer/monomer ratio. (For example: a residence time of 19.5 min was employed for the first block (0.041 mL min^{-1} flow rate 1) and 40 min for the second block (0.049 mL min^{-1} flow rate 2) to develop a P*n*BuA-*b*-PDEGA diblock copolymer.) The results of the systematic study on P*n*BuA-*b*-… diblock copolymers can be found in the main article, while the results on PMA-*b*…, PHEA-*b*-… and PDEGA-*b*-… diblock copolymers are shown below.

Table S1: Diblock copolymers based on PMA as first block, obtained from a [0.8 mL + 3.6 mL] tubular reactor cascade without intermediate purification or isolation. The first block (homopolymer PMA – entry 1) was carried out in the 0.8 mL reactor, with a monomer concentration of 4M, at 100°C and 16 min residence time (19.5 min for entries 7-9). The second block was directly polymerized in the 3.6 mL reactor at 100°C and 40 min residence time.

Entry	**Polymer**	**$[M]_0$ / M**	**Conversion / %**	**$Đ$**	**M_n^{app} / g · mol^{-1}**	**M_p^{app} / g · mol^{-1}**	**M_n^{theor} / g · mol^{-1}**
1	PMA	-	93	1.15	1110	1270	1210
2	PMA-*b*-P*n*BuA	5	90	1.23	1940	2390	2490
3	PMA-*b*-PMA	5	91	1.23	1630	2040	2070
4	PMA-*b*-PEA	5	92	1.22	1770	2190	2210
5	PMA-*b*-P*t*BuA	5	95	1.26	2060	2640	2493
6	PMA-*b*-PHEA	5	96	1.27	1510	2040	2370
7	PMA-*b*-PNIPAM	3.3	96	1.25	1560	1910	2340
8	PMA-*b*-PEHA	3.3	85	1.23	1750	2030	3050
9	PMA-*b*-PDEGA	3.3	84	1.29	2050	2470	3090

Table S2: Diblock copolymers based on PHEA as first block, obtained from a [0.8 mL + 3.6 mL] tubular reactor cascade without intermediate purification or isolation. The first block (homopolymer PHEA –

entry 1) was carried out in the 0.8 mL reactor, with a monomer concentration of 3M, at 100°C and 16 min residence time (17 min for entries 7-9). The second block was directly polymerized in the 3.6 mL reactor at 100°C and 45 min residence time (40.5 min for entries 7-9).

Entry	***Polymer***	**$[M]_0$ / M**	***Conversion* / %**	***Đ***	**M_n^{app} / g · mol^{-1}**	**M_p^{app} / g · mol^{-1}**	**M_n^{theor} / g · mol^{-1}**
1	PHEA	-	98	1.14	1100	1340	1510
2	PHEA-*b*-P*n*BuA	5	92	1.45	1560	2520	2790
3	PHEA-*b*-PMA	5	88	1.32	1290	1930	2370
4	PHEA-*b*-PEA	5	94	1.37	1550	2250	2510
5	PHEA-*b*-P*t*BuA	5	91	1.33	1350	2030	2790
6	PHEA-*b*-PHEA	5	96	1.29	1170	1780	2673
7	PHEA-*b*-PNIPAM	3.3	95	1.34	1330	1820	2640
8	PHEA-*b*-PEHA	3.3	89	1.46	1660	2630	3350
9	PHEA-*b*-PDEGA	3.3	96	1.47	1980	2820	3390

Table S3: Diblock copolymers based on PDEGA as first block, obtained from a [0.8 mL + 3.6 mL] tubular reactor cascade without intermediate purification or isolation. The first block (homopolymer DEGA – entry 1) was carried out in the 0.8 mL reactor, with a monomer concentration of 3M, at 100°C and 16 min residence time (17 min for entries 7-9). The second block was directly polymerized in the 3.6 mL reactor at 100°C and 45 min residence time (40.5 min for entries 7-9).

Entry	***Polymer***	**$[M]_0$ / M**	***Conversion* / %**	***Đ***	**M_n^{app} / g · mol^{-1}**	**M_p^{app} / g · mol^{-1}**	**M_n^{theor} / g · mol^{-1}**
1	PDEGA	-	95	1.16	2031	2378	2230
2	PDEGA-*b*-P*n*BuA	5	85	1.25	2699	3288	3510
3	PDEGA-*b*-PMA	5	89	1.23	2273	2795	3090
4	PDEGA-*b*-PEA	5	83	1.31	2431	3148	3230
5	PDEGA-*b*-P*t*BuA	5	93	1.32	2683	3405	3510
6	PDEGA-*b*-PHEA	5	98	1.22	2296	2250	3390
7	PDEGA-*b*-PNIPAM	3.3	93	1.29	2289	2647	3360
8	PDEGA-*b*-PEHA	3.3	91	1.28	2663	3326	4076
9	PDEGA-*b*-PDEGA	3.3	95	1.37	2837	3594	4110

Diblock copolymers with different monomer/monomer ratios were also targeted by varying flow rate 2 (and adapting the required reactors). For example: a P*n*BuA-*b*-PMA diblock with a "10/20" *n*BuA/MA ratio (DP 10 P*n*BuA block *vs* DP 20 MA block) could be obtained by employing 0.050 mL min^{-1} flow rate of the *n*BuA solution (16 min residence time) and 0.08 mL min^{-1} flow rate of the MA solution (40 min residence time) in a [0.8 mL + 5.2 mL] tubular reactor cascade. Here, 3 types of diblock copolymers were targeted with different monomer/monomer ratios and thus different chain lengths: P*n*BuA-*b*-PMA, P*n*BuA-*b*-PHEA and P*n*BuA-*b*-PDEGA (Table S4).

Table S4. P*n*BuA-*b*-PMA, P*n*BuA-*b*-PHEA and P*n*BuA-*b*-PDEGA diblock copolymers with different monomer/monomer ratios. For the P*n*BuA-*b*-PMA and P*n*BuA-*b*-PHEA diblock copolymers: the first block (homopolymer P*n*BuA) was carried out in the 0.8 mL reactor, with a monomer concentration of 4M, at 100°C and 16 min residence time (26.6 min for 10/40). The second block was directly polymerized in the 3.6 mL reactor, with a monomer concentration of 5M, at 100°C and 40 min residence time (51.4 min for 10/5). For the P*n*BuA-*b*-PDEGA diblock copolymers: the residence times slightly vary: 16 min + 45 min for 10/5, 19.5 min + 40 min for 10/10, 21 min + 40 min for 10/20 and 36.4 min + 40 min for 10/40.

Polymer	***Conversion / %***	***Đ***	**M_n^{app} / g · mol^{-1}**	**M_p^{app} / g · mol^{-1}**	**M_n^{theor} / g · mol^{-1}**
10/5 P*n*BuA-*b*-PMA	84	1.16	1830	2140	2060
10/10 P*n*BuA-*b*-PMA	96	1.21	1950	2450	2490
10/20 P*n*BuA-*b*-PMA	95	1.24	2700	3160	3350
10/40 P*n*BuA-*b*-PMA	96	1.41	3830	4920	5080

Polymer	***Conversion / %***	***Đ***	**M_n^{app} / g · mol^{-1}**	**M_p^{app} / g · mol^{-1}**	**M_n^{theor} / g · mol^{-1}**
10/5 P*n*BuA-*b*-PHEA	91	1.20	1920	2150	2210
10/10 P*n*BuA-*b*-PHEA	97	1.27	1980	2470	2790
10/20 P*n*BuA-*b*-PHEA	98	1.22	2240	2570	3950
10/40 P*n*BuA-*b*-PHEA	97	1.32	2360	3490	6280

Polymer	***Conversion / %***	***Đ***	**M_n^{app} / g · mol^{-1}**	**M_p^{app} / g · mol^{-1}**	**M_n^{theor} / g · mol^{-1}**
10/5 P*n*BuA-*b*-PDEGA	84	1.18	2160	2500	2570
10/10 P*n*BuA-*b*-PDEGA	93	1.26	2800	3310	3510
10/20 P*n*BuA-*b*-PDEGA	95	1.47	3570	4530	5400
10/40 P*n*BuA-*b*-PDEGA	98	2.10	5430	6690	9160

Continuous triblock copolymerizations

The first stock solution was prepared similar to the homopolymerizations. The second stock solution was prepared similar to the diblock copolymerizations, though more AIBN was added (0.45 mmol, 74 mg, 0.09 equiv.). In a third stock solution, 50 mmol (5.006 g, 10 equiv., 5 M) of the monomer EA and 0.65 mmol (107 mg, 0.13 equiv.) of the initiator AIBN were dissolved in *n*-butanol. The solution was kept in a sealed Duran flask at 0°C and protected from light. The solution was connected to the reactor set-up *via* a third HPLC pump and purged with Ar prior to use. A [0.8 mL + 3.6 mL + 5.2 mL] tubular reactor cascade was employed for the polymerizations. By carefully choosing the reactor volume of the third block, and its corresponding flow rate, a 1:1:1 ratio between monomer 1, 2 and 3 could be achieved. Hence, residence times of 16 min, 40 min and 40 min were employed for the first, second and third block respectively (0.050 mL min^{-1} flow rate 1, 0.040 mL min^{-1} flow rate 2 and 0.040mL min^{-1} flow rate 3). Monomer conversions of the third block were determined *via* ^{1}H NMR (92%) and molecular weight distributions were analyzed *via* SEC (2260 g mol^{-1}, $Đ$ = 1.35). Other triblock copolymers could be obtained *via* a similar procedure as described above. Depending on the monomer concentrations, flow rates could be adjusted to assure 1/1/1 monomer/monomer/monomer ratios.

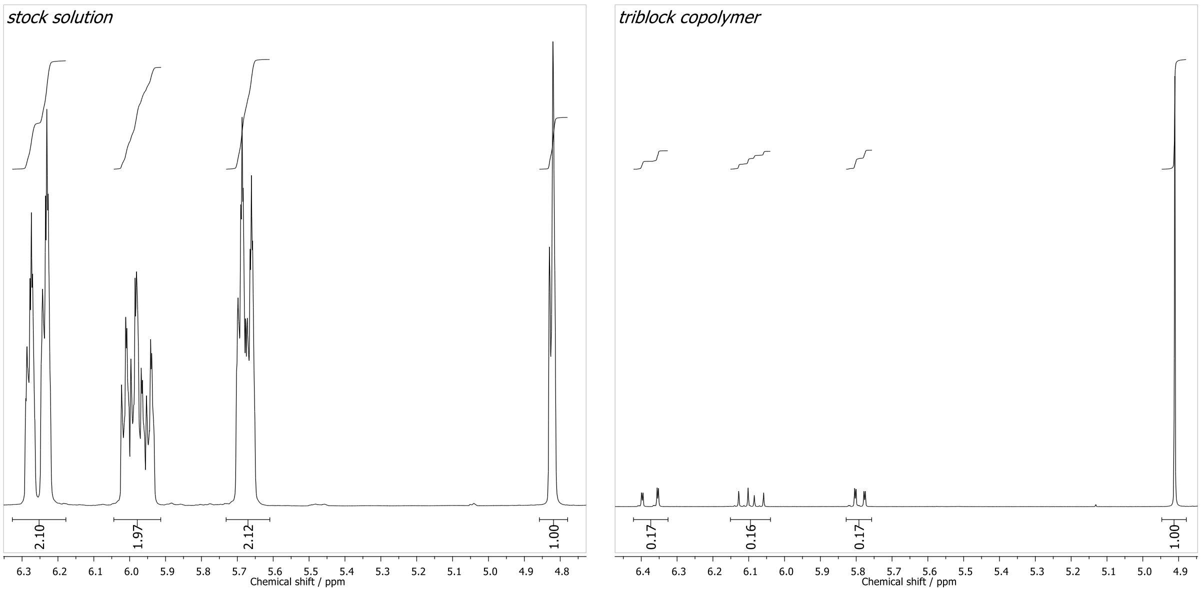
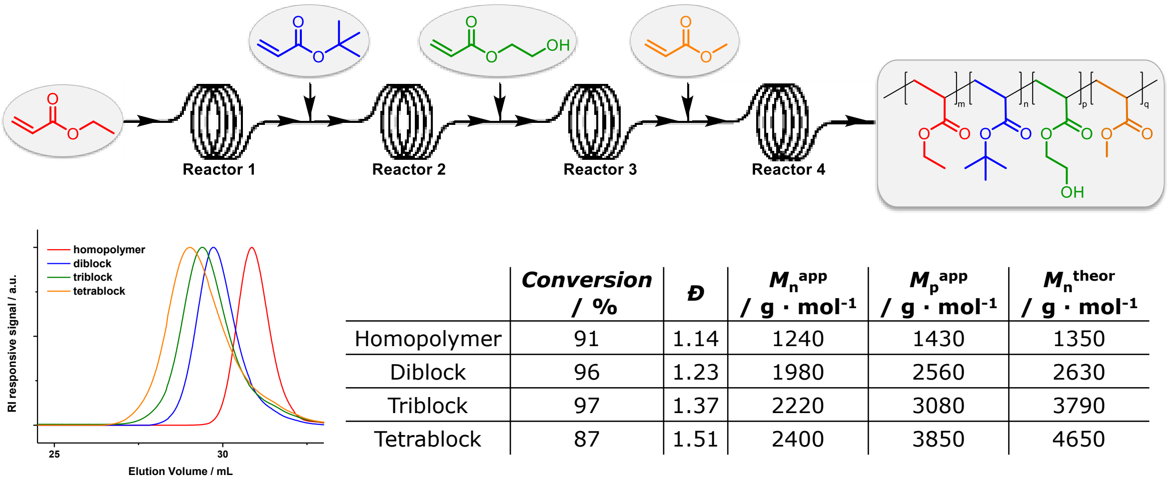


Figure S2. Determination of the monomer conversion of the third block *via* the use of dichloromethane as internal standard in ^{1}H NMR. (Integration of the $C\underline{H_2}Br_2$ peak vs the average integration of the monomer peaks ($C\underline{H_2}=C\underline{H}$-) was compared between the stock solution and the reaction mixture.)

Continuous tetrablock copolymerizations

Other tetrablock copolymers could be targeted as well. As example, also an EA-*b*-*t*BuA-*b*-HEA-*b*-MA tetrablock copolymer was synthesized by employing the same reactor cascade (Figure S3). Yet, depending on the employed monomer concentrations, flow rates must be adjusted to assure a 1:1:1:1 ratio between monomer 1, 2, 3 and 4.



	***Conversion* / %**	***Đ***	***M*$_n$^{app} / g · mol^{-1}**	***M*$_p$^{app} / g · mol^{-1}**	***M*$_n$^{theor} / g · mol^{-1}**
Homopolymer	91	1.14	1240	1430	1350
Diblock	96	1.23	1980	2560	2630
Triblock	97	1.37	2220	3080	3790
Tetrablock	87	1.51	2400	3850	4650

Figure S3: Schematic representation of the synthesis of a PEA-*b*-P*t*BuA-*b*-PHEA-*b*-PMA tetrablock copolymer *via* the use of a [0.8 mL + 3.6 mL + 5.2 mL + 6.8 mL] reactor cascade.