Supporting Information

Synthesis of Sequence-Controlled Acrylate Oligomers via Consecutive RAFT Monomers Additions

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1. Materials

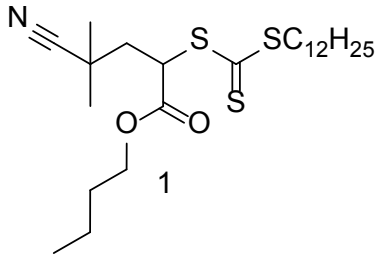
The monomers, *n*-butyl acrylate (Acros, 99%), *t*-butyl acrylate (Acros, 99%) and 2-ethylhexyl acrylate (Acros, 99%) were deinhibited over a column of activated basic alumina, prior to use. 1,1'-azobis(isobutyronitrile) (AIBN, Sigma-Aldrich, 98%) was recrystallized twice from ethanol prior to use. 2-cyano-2-propyl dodecyl trithiocarbonate (CPD-TTC) (Sigma-Aldrich,

97%) was used as received. All solvents used are obtained from commercial sources (Acros and Sigma-Aldrich) and used without further purification.

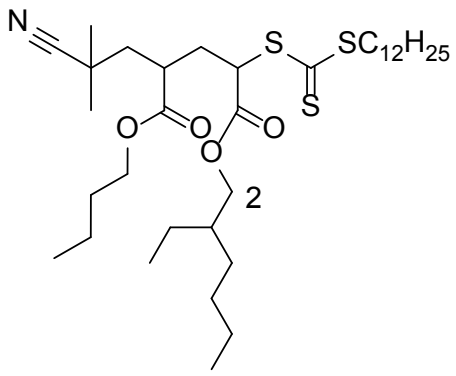
2. Characterization

Purification of products was performed on a recycling preparative HPLC LC-9210 NEXT system in the manual injection mode (3 mL) comprising a JAIGEL-1H and JAIGEL-2H column and a NEXT series UV detector using $CHCl_3$ as the eluent with a flow rate of 3.5 $mL \cdot min^{-1}$. Fractions were collected manually. NMR spectra were recorded in deuterated chloroform with a Varian Inova 300 spectrometer at 300 MHz for ^{1}H NMR and at 75 MHz for ^{13}C NMR using a Varian probe (5 mm-4-nucleus AutoSWPFG) and a pulse delay of 12 s. Analysis of the MWDs of the polymer samples were performed on a Tosoh EcoSEC operated by PSS WinGPC software, equipped with a PLgel 5.0 μm guard column (50 × 8 mm), followed by three PLgel 5 μm Mixed-C columns (300 × 8 mm) and a differential refractive index detector using THF as the eluent at 40 °C with a flow rate of 1 mL min^{-1}. The SEC system was calibrated using linear narrow polystyrene standards ranging from 474 to 7.5 x 10^6 $gmol^{-1}$ PS ($K = 14.1 \times 10^{-5}$ dLg^{-1} and $\alpha = 0.70$), and toluene as a flow marker. ESI-MS was performed using an LCQ Fleet mass spectrometer (ThermoFischer Scientific) equipped with an atmospheric pressure ionization source operating in the nebulizer assisted electro spray mode. The instrument was calibrated in the m/z range 220-2000 using a standard solution containing caffeine, MRFA and Ultramark 1621. A constant spray voltage of 5 kV was used and nitrogen at a dimensionless auxiliary gas flow-rate of 3 and a dimensionless sheath gas flow-rate of 3 were applied. The capillary voltage, the tube lens offset voltage and the capillary temperature were set to 25 V, 120 V, and 275°C respectively. A 250 μL aliquot of a polymer solution with concentration of 10 μg mL^{-1} was injected. A mixture of THF and methanol (THF:MeOH = 3:2), all HPLC grade, were used as solvent.

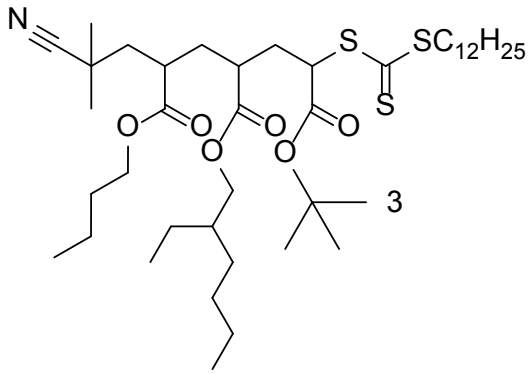
3. Synthetic Procedures



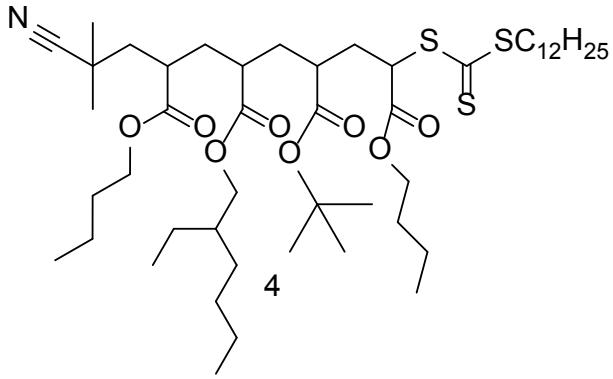
***n*BuA RAFT agent (1).** In a typical procedure, 15.604 mmol (2.00 g, 10 equiv) of the monomer *n*-BuA, 0.078 mmol (0.013 g, 0.05 equiv) of AIBN, 1.560 mmol (0.540 g, 1 equiv) of 2-cyano-2-propyl dodecyl trithiocarbonate (CPD-TTC) RAFT agent and 2 mL of butyl acetate were added into a sealed Schlenk tube. The schlenk tube was subjected to 3 freeze-pump-thaw cycles, and subsequently inserted into the glovebox. The schlenk tube was opened and the mixture was transferred into a glass vial with a stirring bar inside. The glass vial was placed in a copper heat-block of 100 °C. The mixture was reacted for 10 min at 100 °C and subsequently quenched by cooling the vial in liquid nitrogen and subjecting to ambient atmosphere. Subsequently the mixture was transferred into an aluminium pan to evaporate excess of solvent and monomer, yielding 0.690 g of crude product mixture. The mixture was purified via recycling SEC to yield 0.410 g (55%) of pure *n*BuA oligo-RAFT agent (**1**). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 5.00−4.90 (dd, J = 9.7 and 4.5 Hz, 1H, CHCOO, backbone), 4.20−4.10 (t, J = 6.6 Hz, 2H, $CH_2OC{=}O$, side chain), 3.40−3.30 (t, J = 7.5 Hz, 2H, $CH_2SC{=}S$, chain end), 2.46−2.40 (dd, J = 14.4. and 9.7 Hz, 1H, C$\underline{H}_2$CH, backbone), 2.04−1.96 (dd, J = 14.4 and 4.5 Hz, 1H, C$\underline{H}_2$CH, backbone), 1.72−1.57 (m, 2H, CH_2, side chain + 2H, CH_2, chain end), 1.45 (s, 3H, CN-C-CH_3), 1.42−1.32 (b, 2H, CH_2, side chain + 2H, CH_2, chain end + 3H, CN-C-CH_3), 1.30−1.20 (b, 16H, CH_2, chain end), 0.93−0.88 (t, J = 7.4 Hz, 3H, CH_3, side chain), 0.88−0.83 (t, J = 6.9 Hz, 3H, CH_3, chain end). ESI-MS (m/z): 496.25 ($M+Na^+$).



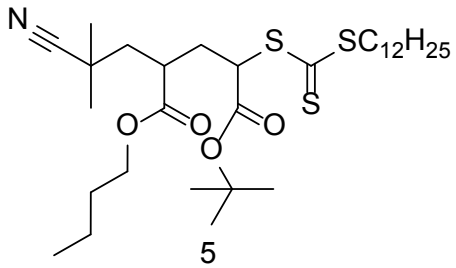
***n*BuA-EHA RAFT agent (2).** In a typical procedure, 0.317 mmol (0.058 g, 1 equiv) of the monomer EHA, 0.016 mmol (2.600 mg, 0.05 equiv) of AIBN, 0.317 mmol (0.150 g, 1 equiv) of *n*BuA macro-RAFT agent (**1**) and 0.6 mL of butyl acetate were added into a 1.5mL glass vial. The mixture was degassed for 10 min with nitrogen purging, after which the vial was inserted into the glovebox. A stirring bar was added and the vial was placed in a copper heat-block at 100 °C. The mixture was reacted for 10 min at 100 °C and subsequently quenched by cooling the vial in liquid nitrogen and subjecting to ambient atmosphere. Subsequently excess of solvent and monomer were evaporated from the vial. The crude mixture was purified via recycling SEC to yield 0.096 g (46%) of pure *n*BuA-EHA macro-RAFT agent (**2**). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.95−4.82 (m, 1H, CHCOO, backbone, EHA unit), 4.20−3.95 (m, 4H, $CH_2OC{=}O$, side chains), 3.40−3.15 (d t, J = 7.5 Hz, 2H, $CH_2SC{=}S$, chain end), 2.81−2.66 (b, 1H, CHCOO, backbone, *n*BuA unit), 2.46−1.94 (b, 4H, $C\underline{H_2}CHC\underline{H_2}CH$, backbone), 1.72−1.52 (m, 2H, CH_2, *n*BuA side chain + 1H, CH, EHA side chain + 2H, CH_2, chain end), 1.45−1.20 (b, 10H, CH_2, side chains + 18H, CH_2, chain end + 6H, CN-C-$(CH_3)_2$), 0.97−0.91 (t, J = 7.4 Hz, 3H, CH_3, *n*BuA side chain), 0.91−0.83 (b, 3H, CH_3, chain end + 6H, CH_3, EHA side chain). ESI-MS (m/z): 680.33 ($M+Na^+$).



***n*BuA-EHA-*t*BuA RAFT agent (3).** The same procedure as for synthesis of **2** was applied, using 0.146 mmol (0.019 g, 1 equiv) of the monomer *t*BuA, 0.007 mmol (1.200 mg, 0.05 equiv) of AIBN, 0.146 mmol (0.096 g, 1 equiv) of *n*BuA-EHA macro-RAFT agent (**2**) and 0.3 mL of butyl acetate. After reaction the crude mixture was purified via recycling SEC to yield 0.023 g (20%) of pure *n*BuA-EHA-*t*BuA macro-RAFT agent (**3**). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.79−4.63 (m, 1H, CHCOO, backbone, *t*BuA unit), 4.20−3.90 (m, 4H, $CH_2OC{=}O$, side chains), 3.38−3.15 (d t, J = 7.5 Hz, 2H, $CH_2SC{=}S$, chain end), 2.65−2.41 (b, 2H, CHCOO, backbone, *n*BuA and EHA units), 2.42−1.80 (b, 6H, C<u>H$_2$</u>CHC<u>H$_2$</u>CHC<u>H$_2$</u>CH, backbone), 1.72−1.52 (m, 2H, CH_2, *n*BuA side chain + 1H, CH, EHA side chain + 2H, CH_2, chain end), 1.46−1.41 (tr s, 9H, $OC(CH_3)_3$, *t*BuA), 1.42−1.20 (b, 10H, CH_2, side chains + 18H, CH_2, chain end + 6H, CN-C-$(CH_3)_2$), 0.97−0.83 (b, 3H, CH_3, chain end + 3H, CH_3, *n*BuA side chain + 6H, CH_3, EHA side chain). ESI-MS (m/z): 808.25 ($M+Na^+$).

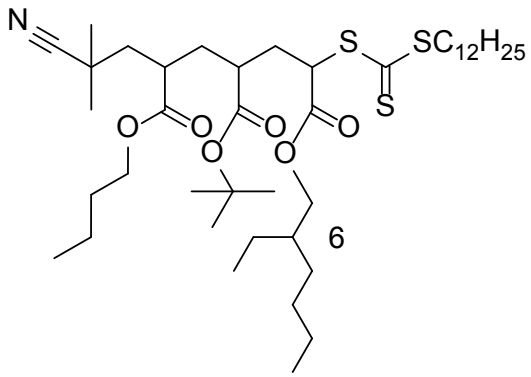


***n*BuA-EHA-*t*BuA-*n*BuA RAFT agent (4).** The same procedure as for synthesis of **2** was applied, using 0.029 mmol (3.750 mg, 1 equiv) of the monomer *n*BuA, 0.0015 mmol (0.240 mg, 0.05 equiv) of AIBN, 0.029 mmol (0.023 g, 1 equiv) of *n*BuA-EHA-*t*BuA macro-RAFT agent (**3**) and 0.1 mL of butyl acetate. After reaction the crude mixture was purified via recycling SEC to yield 1.000 mg (4%) of pure *n*BuA-EHA-*t*BuA-*n*BuA macro-RAFT agent (**4**). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.79−4.63 (m, 1H, CHCOO, backbone, *n*BuA unit), 4.20−3.90 (m, 6H, $CH_2OC{=}O$, side chains), 3.38−3.15 (d t, J = 7.5 Hz, 2H, $CH_2SC{=}S$, chain end), 2.65−2.30 (b, 3H, CHCOO, backbone, *n*BuA, EHA and *t*BuA units), 2.42−1.70 (b, 8H, $C\underline{H_2}CHC\underline{H_2}CHC\underline{H_2}CHC\underline{H_2}CH$, backbone), 1.72−1.52 (m, 4H, CH_2, *n*BuA side chains + 1H, CH, EHA side chain + 2H, CH_2, chain end), 1.46−1.41 (tr s, 9H, $OC(CH_3)_3$, *t*BuA), 1.42−1.20 (b, 12H, CH_2, side chains + 18H, CH_2, chain end + 6H, CN-C-$(CH_3)_2$), 0.97−0.83 (b, 3H, CH_3, chain end + 6H, CH_3, *n*BuA side chains + 6H, CH_3, EHA side chain). ESI-MS (m/z): 936.42 ($M+Na^+$).

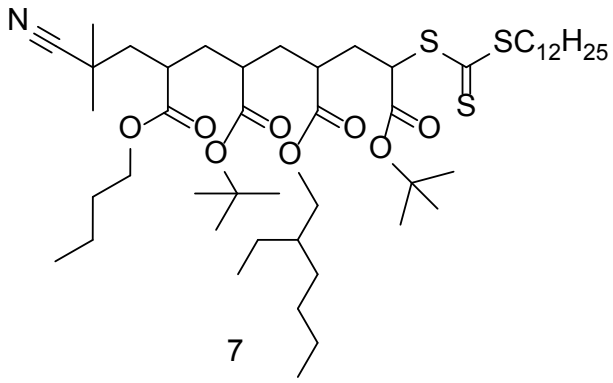


***n*BuA-*t*BuA RAFT agent (5).** The same procedure as for synthesis of **2** was applied, using 0.549 mmol (0.070 g, 1 equiv) of the monomer *t*BuA, 0.027 mmol (4.500 mg, 0.05 equiv) of AIBN, 0.549 mmol (0.260 g, 1 equiv) of *n*BuA macro-RAFT agent (**1**) and 0.8 mL of butyl acetate. After reaction the crude mixture was purified via recycling SEC to yield 0.165 g (50%) of pure *n*BuA-*t*BuA macro-RAFT agent (**5**). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.79−4.63 (m, 1H, CHCOO, backbone, *t*BuA unit), 4.23−4.00 (m, 2H, $CH_2OC{=}O$, side chain), 3.38−3.15 (d t, J = 7.5 Hz, 2H, $CH_2SC{=}S$, chain end), 2.80−2.65 (b, 1H, CHCOO,

backbone, *n*BuA unit), 2.42−1.80 (b, 4H, C<u>H$_2$</u>CHC<u>H$_2$</u>CH, backbone), 1.72−1.57 (m, 2H, CH_2, *n*BuA side chain + 2H, CH_2, chain end), 1.46−1.41 (tr s, 9H, $OC(CH_3)_3$, *t*BuA), 1.42−1.16 (b, 2H, CH_2, *n*BuA side chain + 18H, CH_2, chain end + 6H, CN-C-$(CH_3)_2$), 0.97−0.83 (b, 3H, CH_3, chain end + 3H, CH_3, *n*BuA side chain). ESI-MS (m/z): 624.08 ($M+Na^+$).



***n*BuA-*t*BuA-EHA RAFT agent (6).** The same procedure as for synthesis of **2** was applied, using 0.274 mmol (0.051 g, 1 equiv) of the monomer EHA, 0.014 mmol (2.250 mg, 0.05 equiv) of AIBN, 0.274 mmol (0.165 g, 1 equiv) of *n*BuA-*t*BuA macro-RAFT agent (**5**) and 0.6 mL of butyl acetate. After reaction the crude mixture was purified via recycling SEC to yield 0.044 g (20%) of pure *n*BuA-*t*BuA-EHA macro-RAFT agent (**6**). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.79−4.63 (m, 1H, CHCOO, backbone, EHA unit), 4.20−3.90 (m, 4H, $CH_2OC{=}O$, side chains), 3.38−3.15 (d t, J = 7.5 Hz, 2H, $CH_2SC{=}S$, chain end), 2.65−2.41 (b, 2H, CHCOO, backbone, *n*BuA and *t*BuA units), 2.42−1.70 (b, 6H, C<u>H$_2$</u>CHC<u>H$_2$</u>CHC<u>H$_2$</u>CH, backbone), 1.72−1.52 (m, 2H, CH_2, *n*BuA side chain + 1H, CH, EHA side chain + 2H, CH_2, chain end), 1.46−1.41 (tr s, 9H, $OC(CH_3)_3$, *t*BuA), 1.42−1.20 (b, 10H, CH_2, side chains + 18H, CH_2, chain end + 6H, CN-C-$(CH_3)_2$), 0.97−0.83 (b, 3H, CH_3, chain end + 3H, CH_3, *n*BuA side chain + 6H, CH_3, EHA side chain). ESI-MS (m/z): 808.25 ($M+Na^+$).



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***n*BuA-*t*BuA-EHA-*t*BuA RAFT agent (7).** The same procedure as for synthesis of **2** was applied, using 0.056 mmol (7.200 mg, 1 equiv) of the monomer *t*BuA, 0.0028 mmol (0.460 mg, 0.05 equiv) of AIBN, 0.056 mmol (0.044 g, 1 equiv) of *n*BuA-*t*BuA-EHA macro-RAFT agent (**6**) and 0.1 mL of butyl acetate. After reaction the crude mixture was purified via recycling SEC to yield 6 mg (12%) of pure *n*BuA-*t*BuA-EHA-*t*BuA macro-RAFT agent (**7**). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.79−4.63 (m, 1H, CHCOO, backbone, *t*BuA unit), 4.20−3.90 (m, 4H, $CH_2OC{=}O$, side chains), 3.38−3.15 (d t, J = 7.5 Hz, 2H, $CH_2SC{=}S$, chain end), 2.65−2.41 (b, 3H, CHCOO, backbone, *n*BuA, *t*BuA and EHA units), 2.42−1.70 (b, 8H, $C\underline{H_2}CHC\underline{H_2}CHC\underline{H_2}CHCHC\underline{H_2}$, backbone), 1.72−1.52 (m, 2H, CH_2, *n*BuA side chain + 1H, CH, EHA side chain + 2H, CH_2, chain end), 1.50−1.41 (m, 18H, $OC(CH_3)_3$ tBuA), 1.42−1.20 (b, 10H, CH_2, side chains + 18H, CH_2, chain end + 6H, CN-C-$(CH_3)_2$), 0.97−0.83 (b, 3H, CH_3, chain end + 3H, CH_3, *n*BuA side chain + 6H, CH_3, EHA side chain). ESI-MS (m/z): 936.42 ($M+Na^+$).

4. Spectroscopic Data

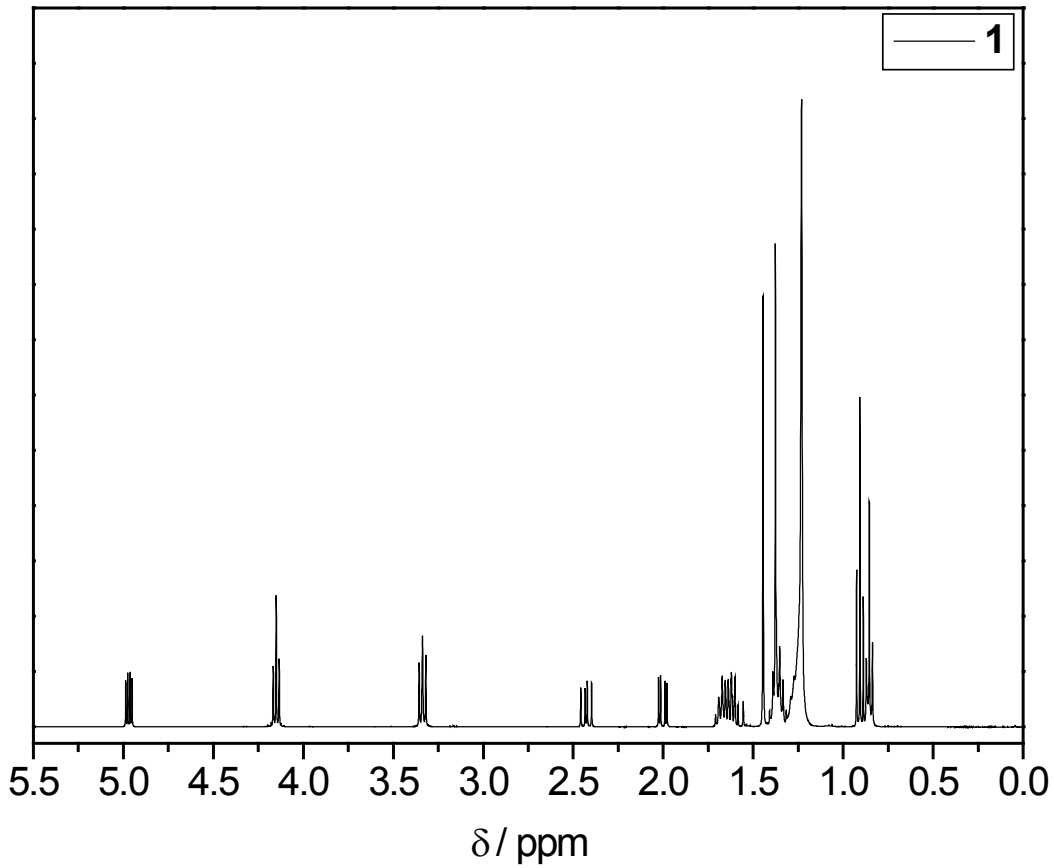

Figure S1. ^{1}H NMR spectrum of *n*BuA RAFT agent **1**.

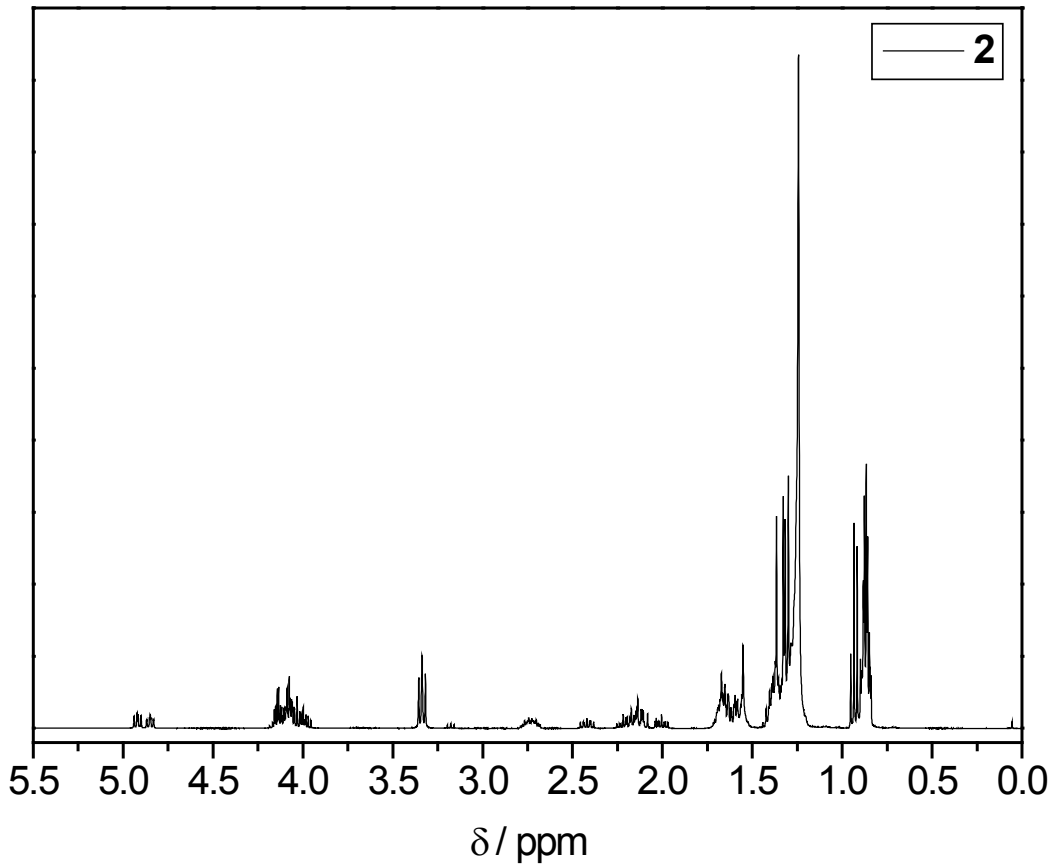

Figure S2. ^{1}H NMR spectrum of *n*BuA-EHA RAFT agent **2**.

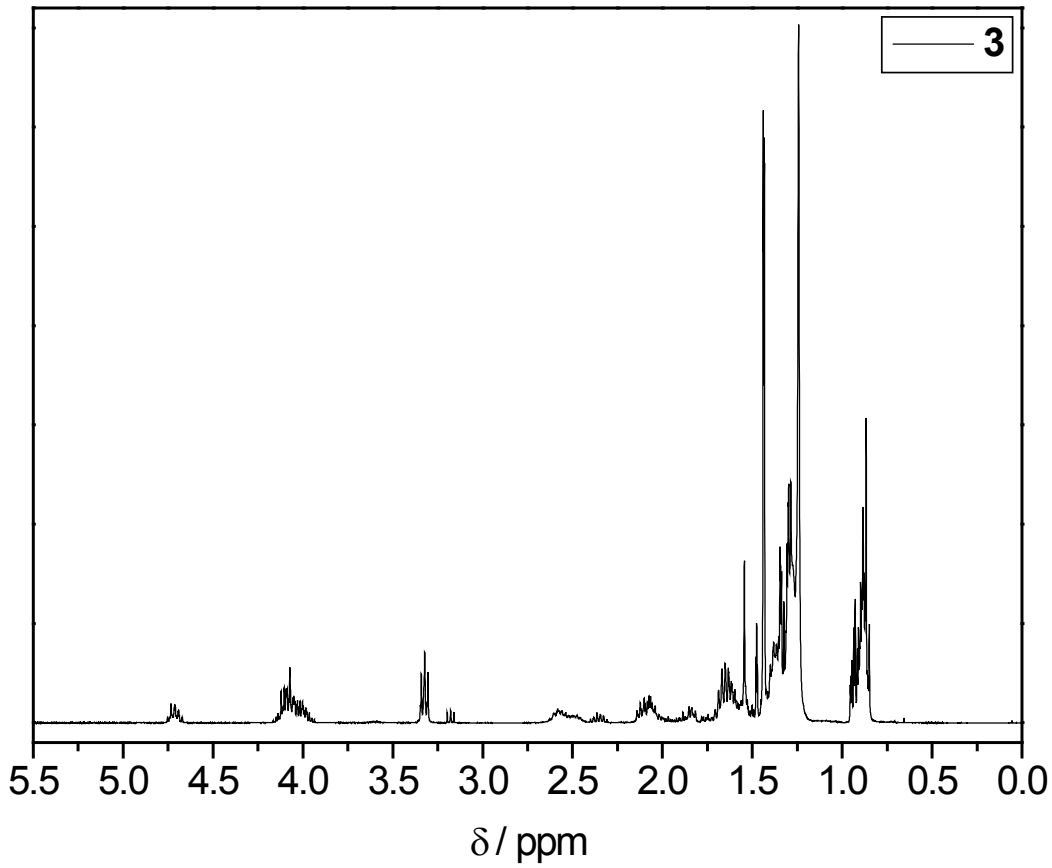

Figure S3. ^{1}H NMR spectrum of *n*BuA-EHA-*t*BuA RAFT agent **3**.

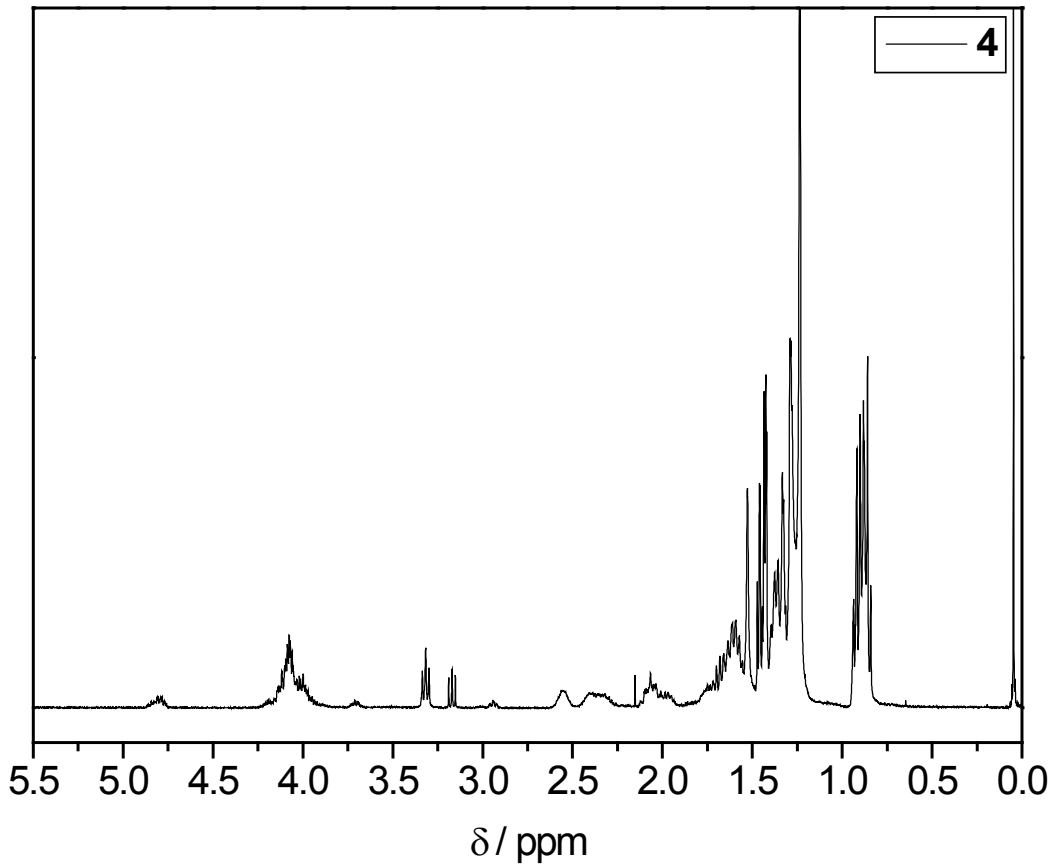

Figure S4. ^{1}H NMR spectrum of *n*BuA-EHA-*t*BuA-*n*BuA RAFT agent **4**.

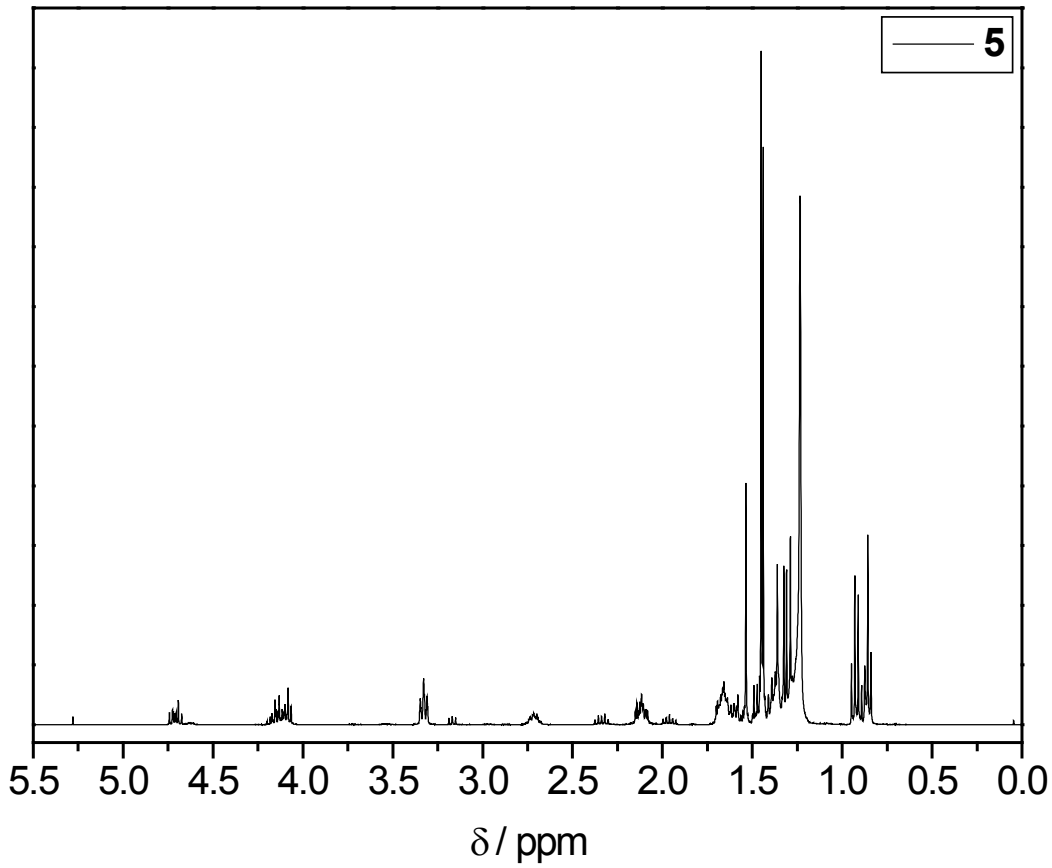

Figure S5. ^{1}H NMR spectrum of *n*BuA-*t*BuA RAFT agent **5**.

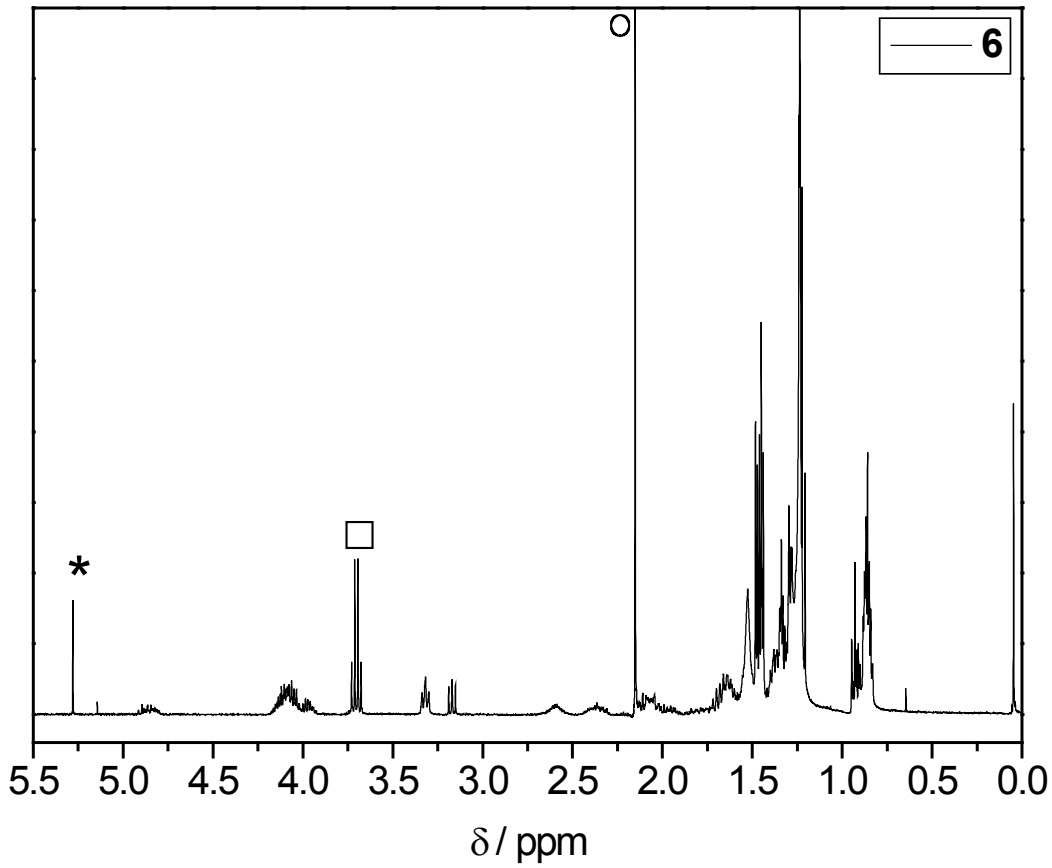

Figure S6. ^{1}H NMR spectrum of *n*BuA-*t*BuA-EHA RAFT agent **6**. The resonances marked with an asterisk, a square and a circle result respectively from $CHCl_2$, EtOH and Acetone leftovers used for cleaning of the NMR tube.

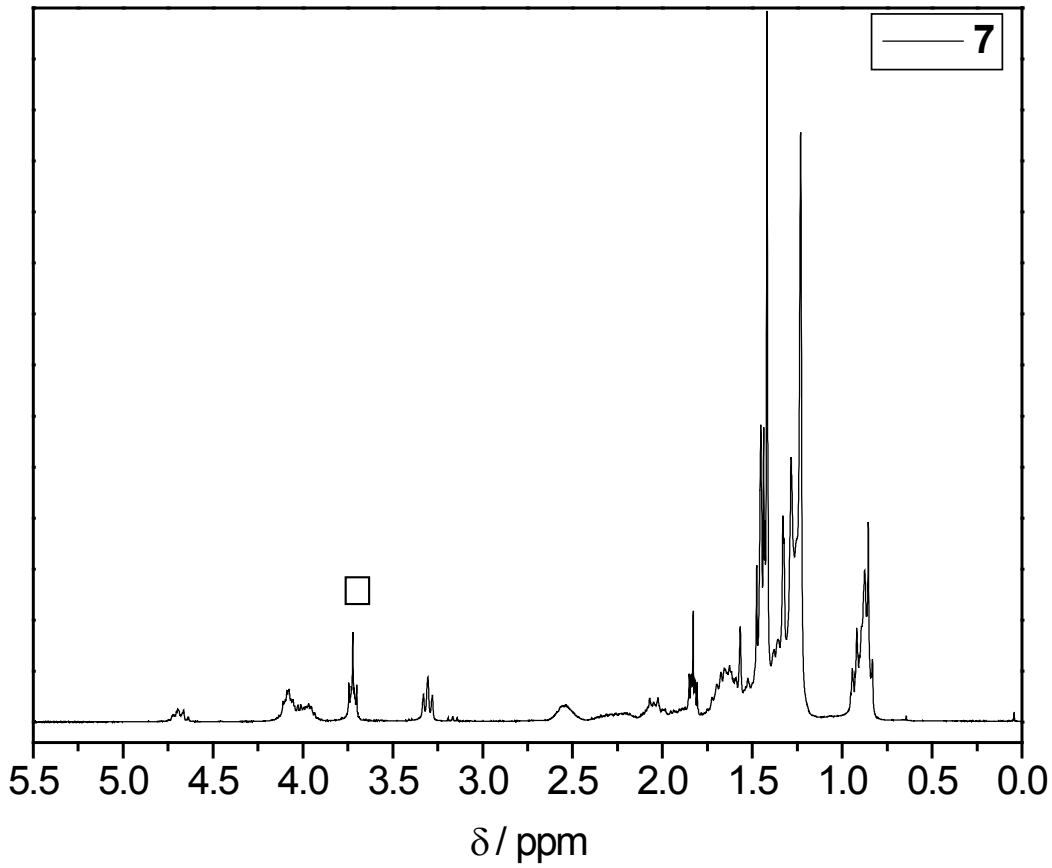

Figure S7. ^{1}H NMR spectrum of *n*BuA-*t*BuA-EHA-*t*BuA RAFT agent **7**. The resonance marked with a square results from EtOH leftovers used for cleaning of the NMR tube.

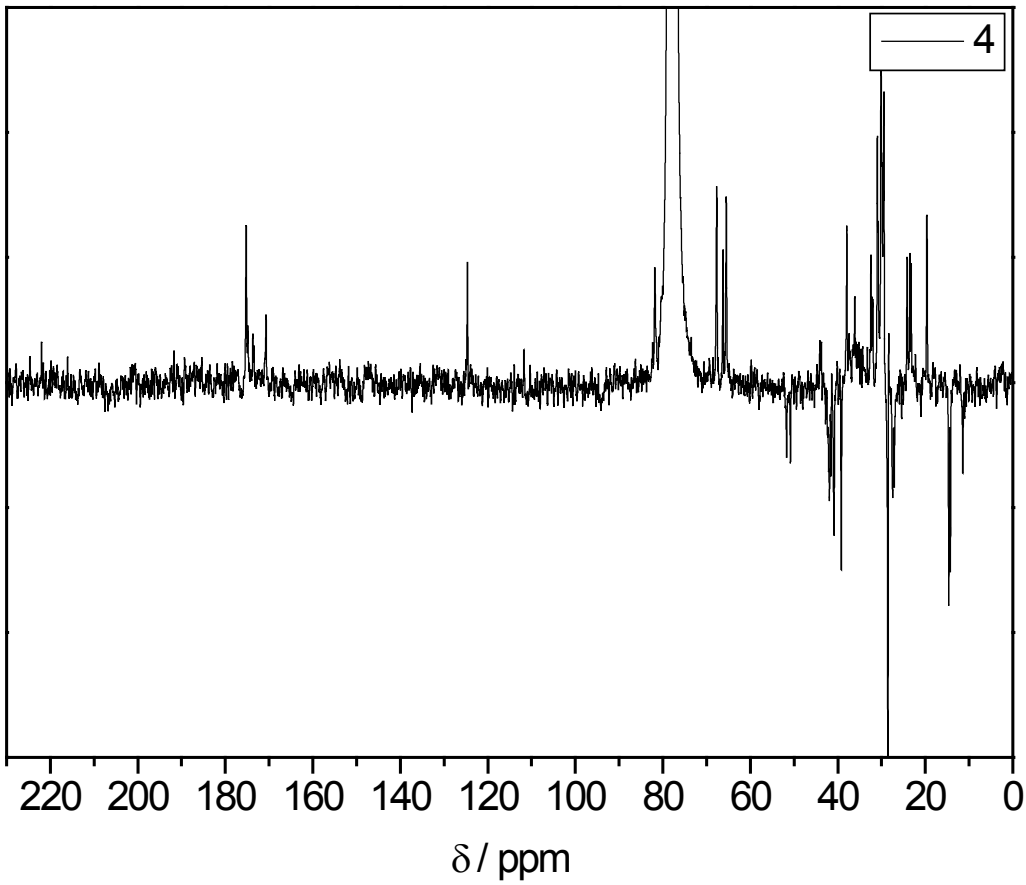

Figure S8. APT ^{13}C NMR spectrum of *n*BuA-EHA-*t*BuA-*n*BuA RAFT agent **4**.

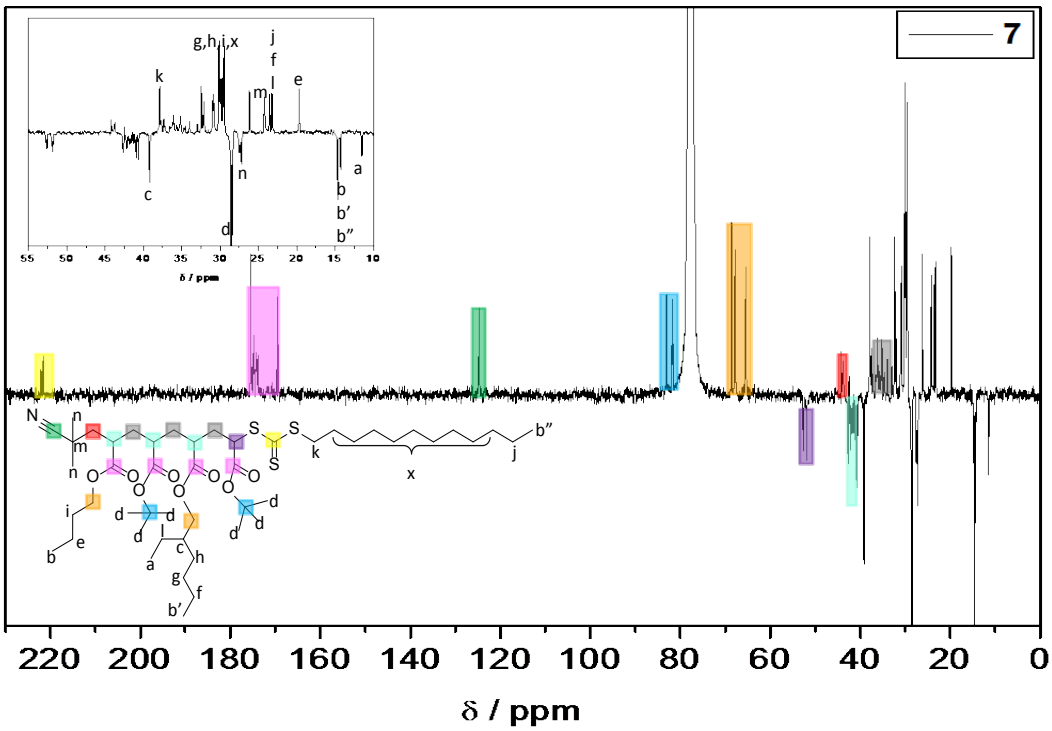

Figure S9. APT ^{13}C NMR spectrum of oligo-RAFT agent **7**.

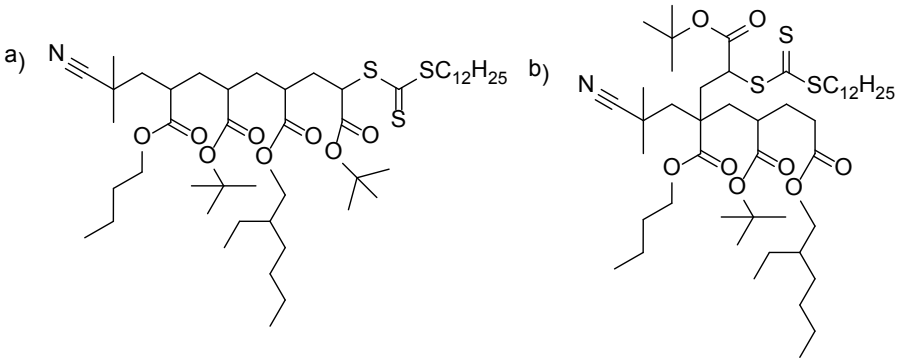

Figure S10. a) Linear backbone of oligo-RAFT agent **7**, b) branched backbone due to presence of mid chain radical caused via backbiting.

Remark: If a branched structure was formed, then the CH_2 carbon next to the resulting methacrylate-like quaternary substituted carbon would give rise to a positive resonance around 52-54 ppm.

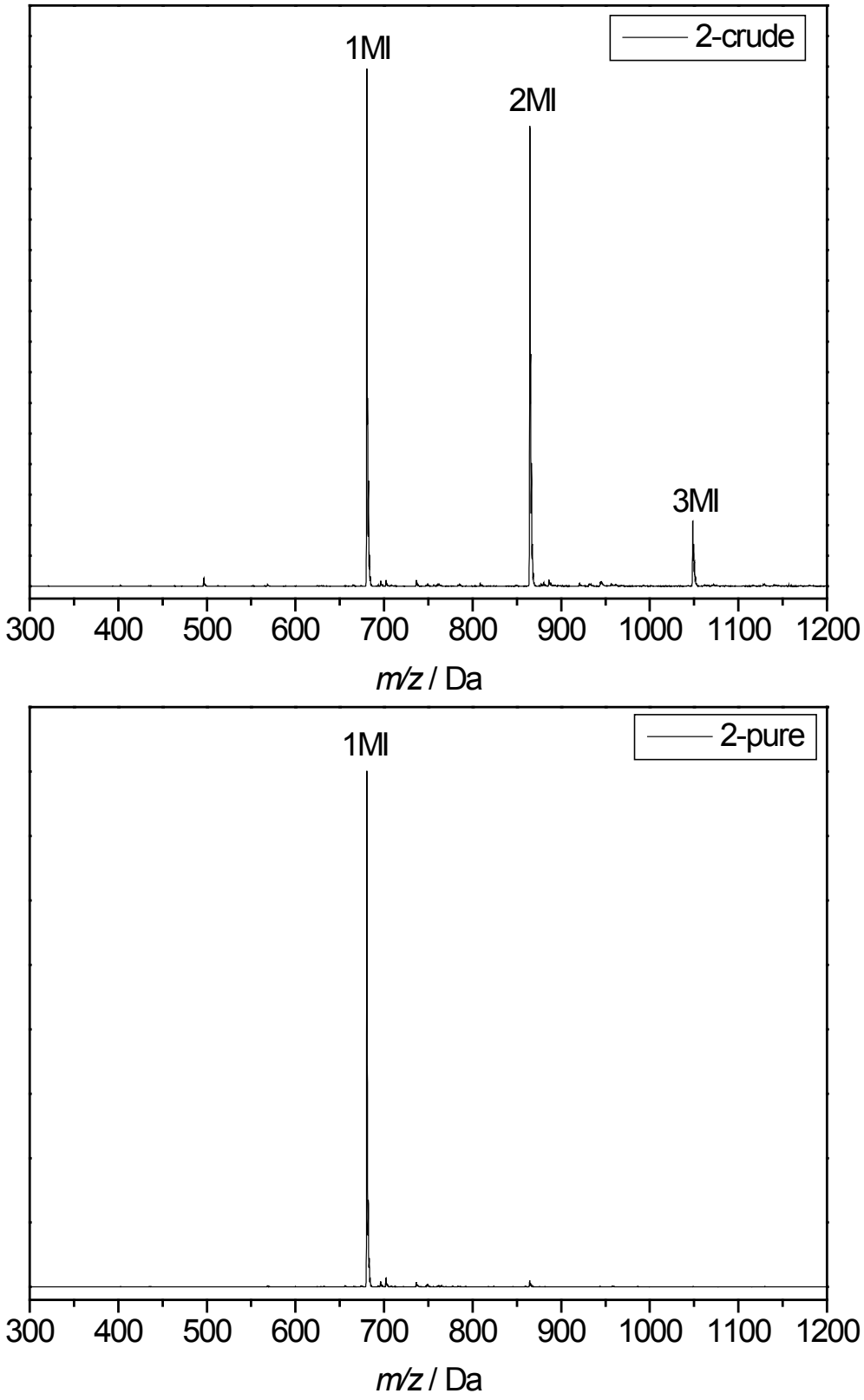

Figure S11. ESI-MS spectra of *n*BuA-EHA RAFT agent **2**, before and after purification with recycling SEC.

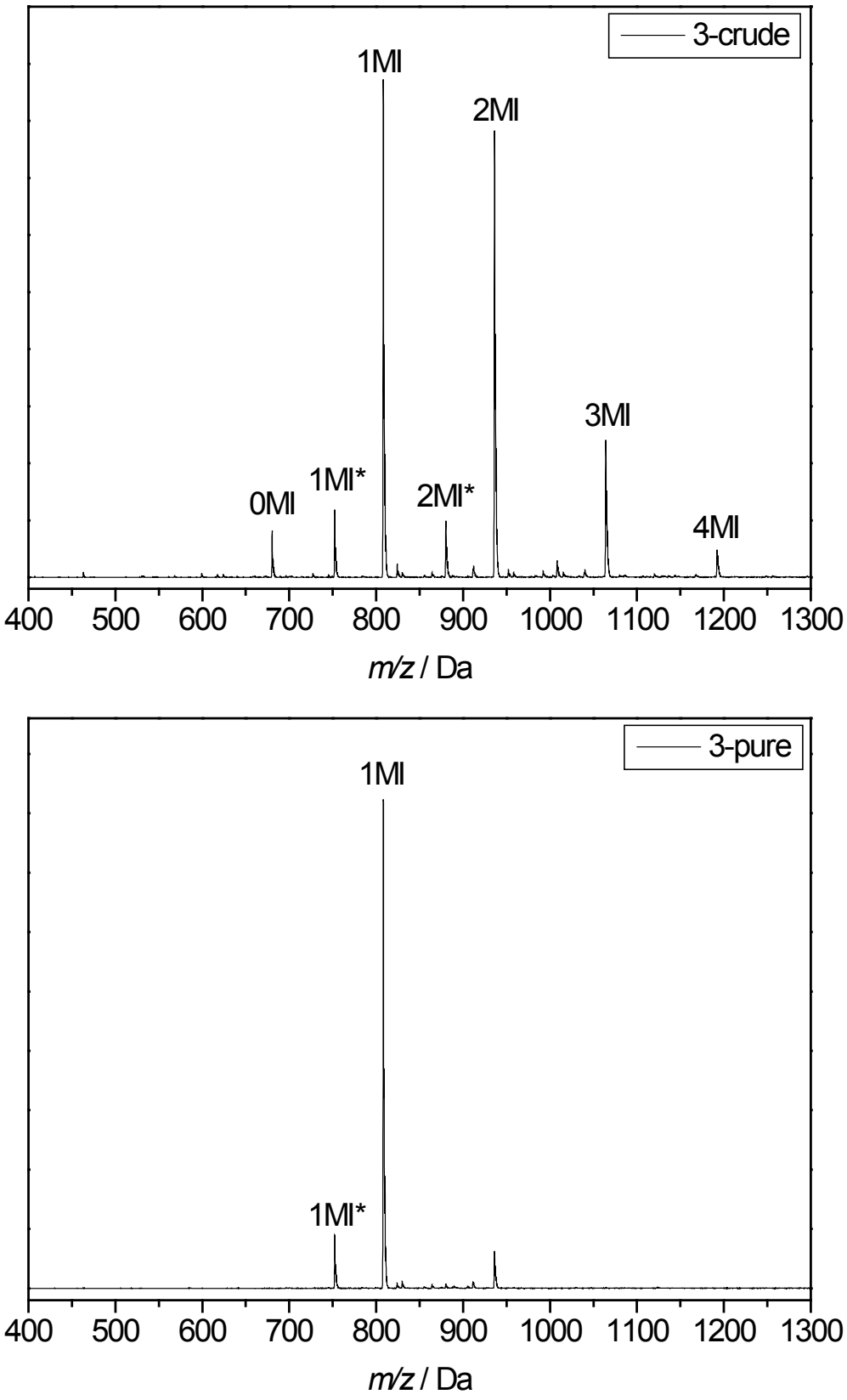

Figure S12. ESI-MS spectra of *n*BuA-EHA-*t*BuA RAFT agent **3**, before and after purification with recycling SEC. Peaks assigned with an asterisk correspond to a monomer insertion product where the *t*BuA group has hydrolyzed into acrylic acid.

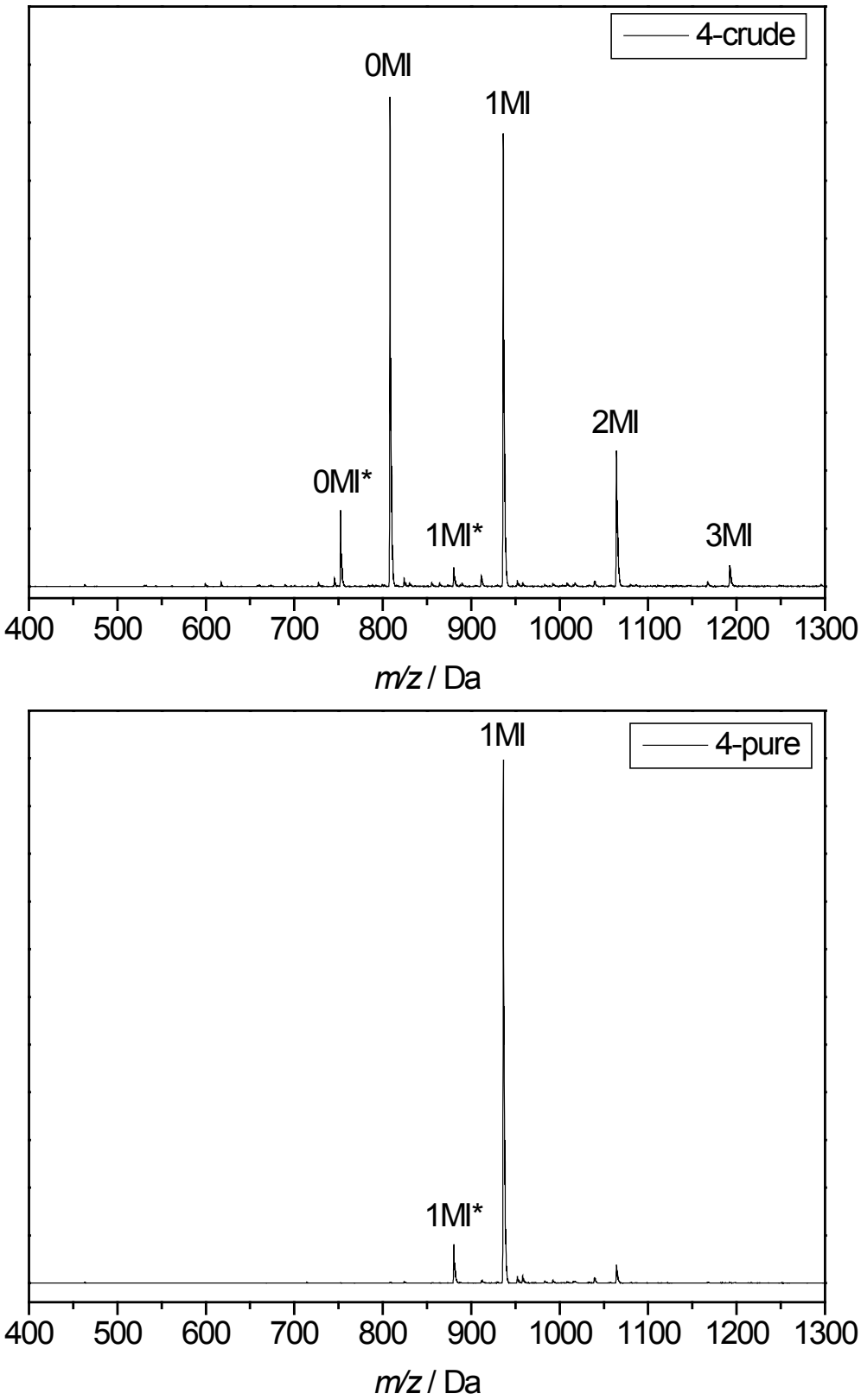

Figure S13. ESI-MS spectra of *n*BuA-EHA-*t*BuA-*n*BuA RAFT agent **4**, before and after purification with recycling SEC. Peaks assigned with an asterisk correspond to a monomer insertion product where the *t*BuA group has hydrolyzed into acrylic acid.

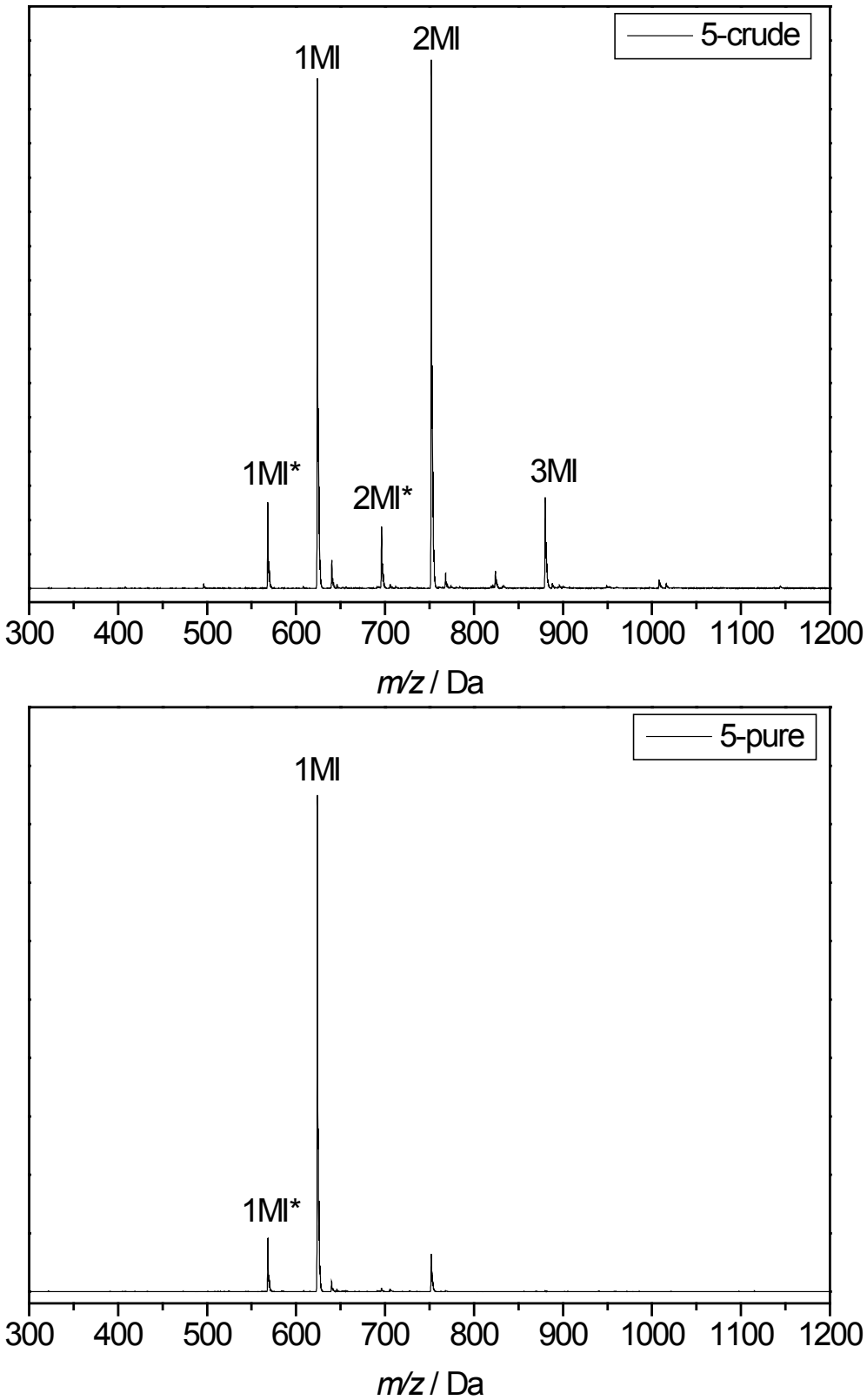

Figure S14. ESI-MS spectra of *n*BuA-*t*BuA RAFT agent **5**, before and after purification with recycling SEC. Peaks assigned with an asterisk correspond to a monomer insertion product where the *t*BuA group has hydrolyzed into acrylic acid.

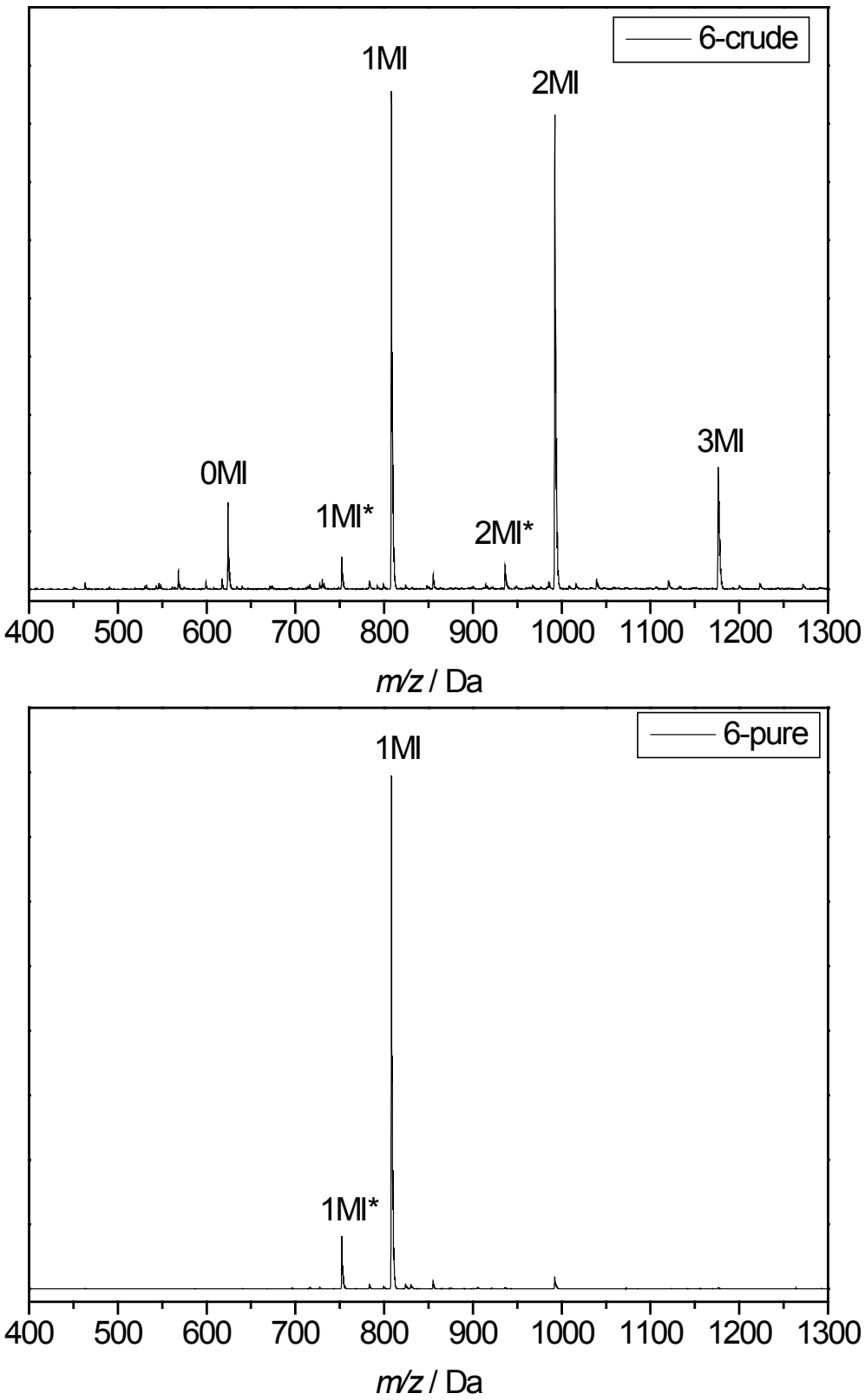

Figure S15. ESI-MS spectra of *n*BuA-*t*BuA-EHA RAFT agent **6**, before and after purification with recycling SEC. Peaks assigned with an asterisk correspond to a monomer insertion product where the *t*BuA group has hydrolyzed into acrylic acid.

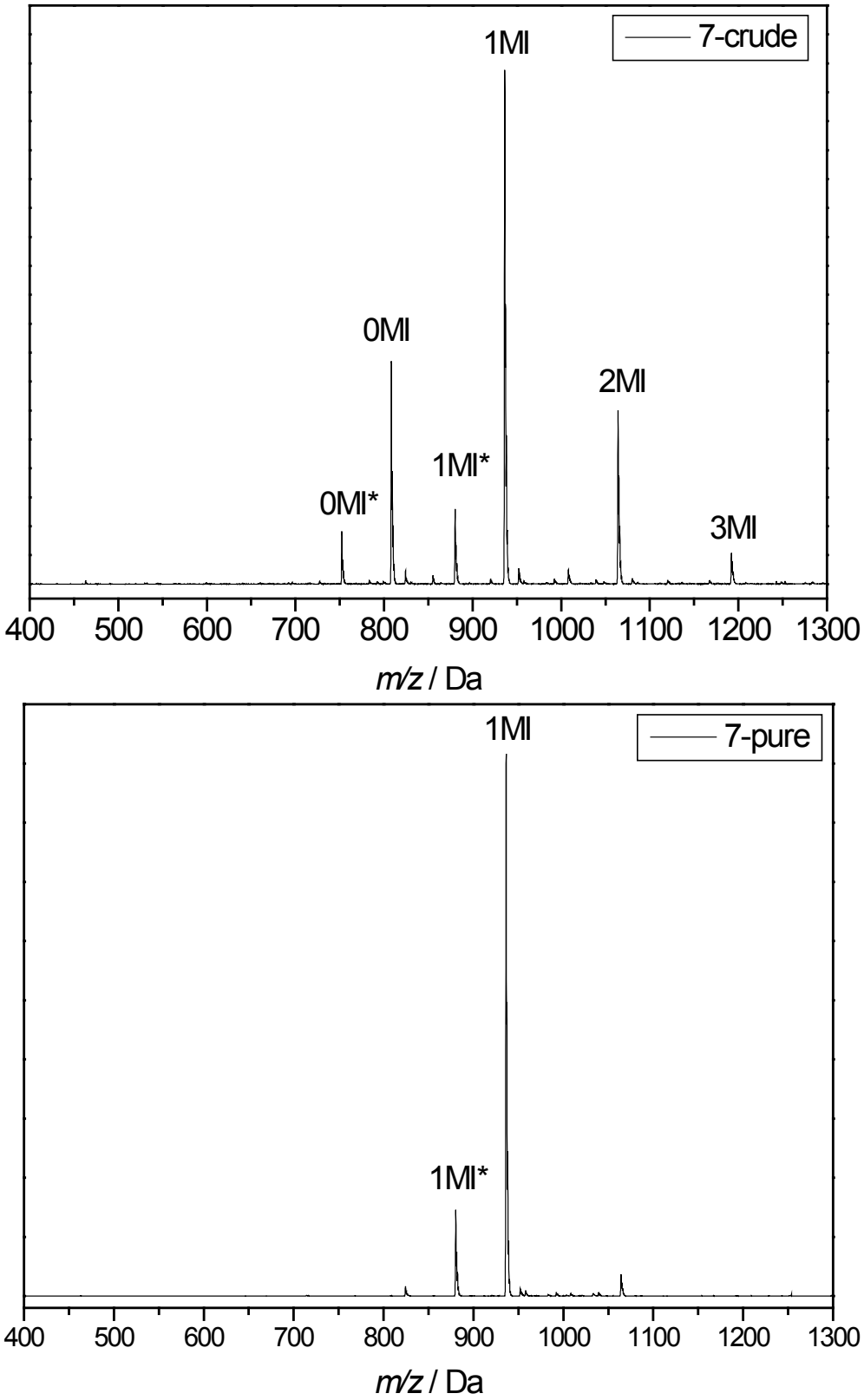

Figure S16. ESI-MS spectra of *n*BuA-*t*BuA-EHA-*t*BuA RAFT agent **7**, before and after purification with recycling SEC. Peaks assigned with an asterisk correspond to a monomer insertion product where the *t*BuA group has hydrolyzed into acrylic acid.

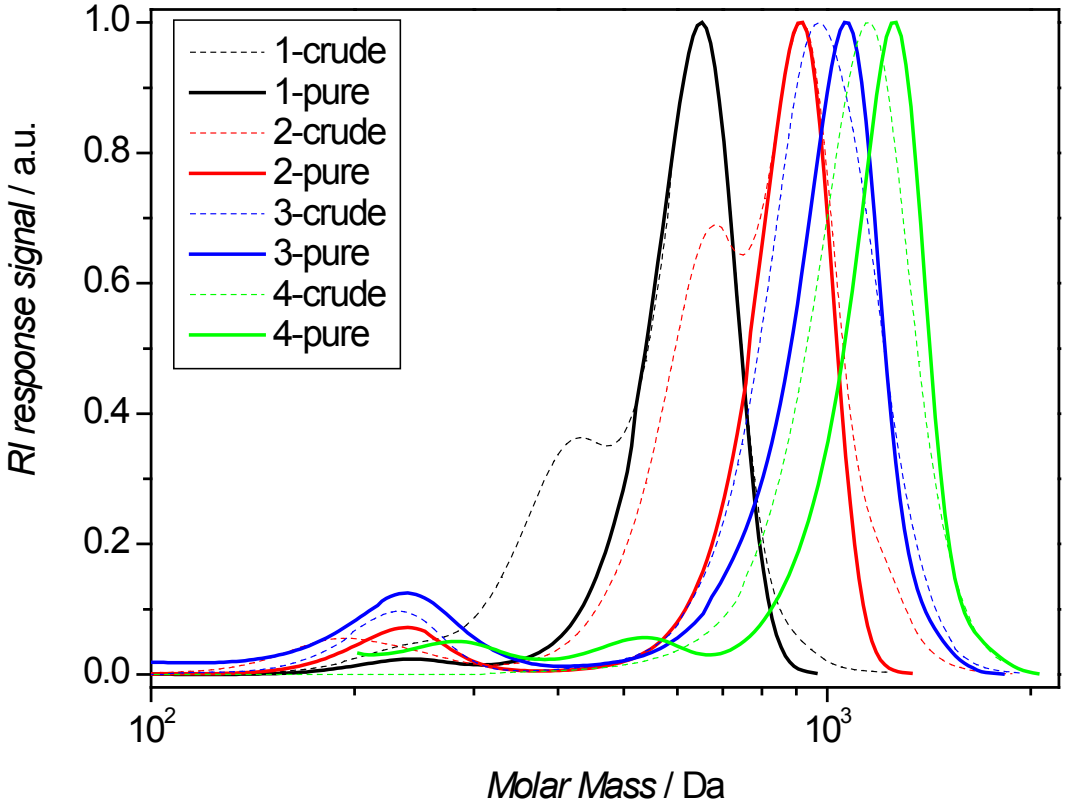

Figure S17. SEC chromatograms of RAFT agents **1**, **2**, **3** and **4**, before (dashed) and after purification (solid) with recycling SEC.

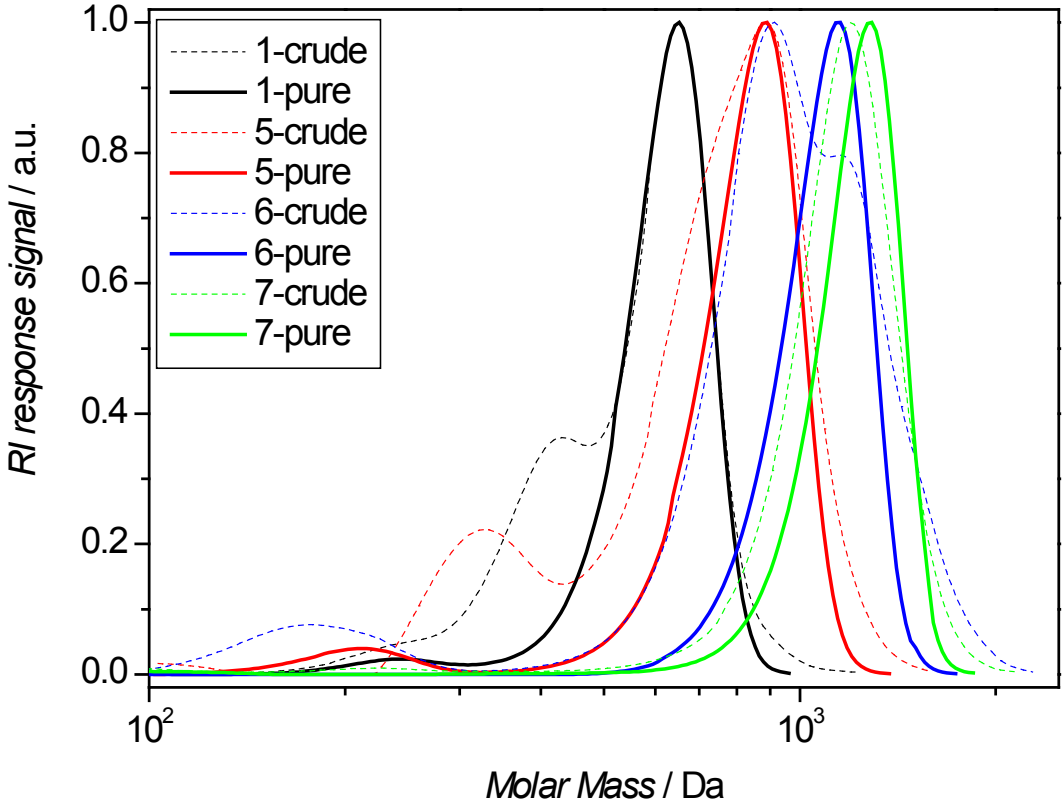

Figure S18. SEC chromatograms of RAFT agents **1**, **5**, **6** and **7**, before (dashed) and after purification (solid) with recycling SEC.

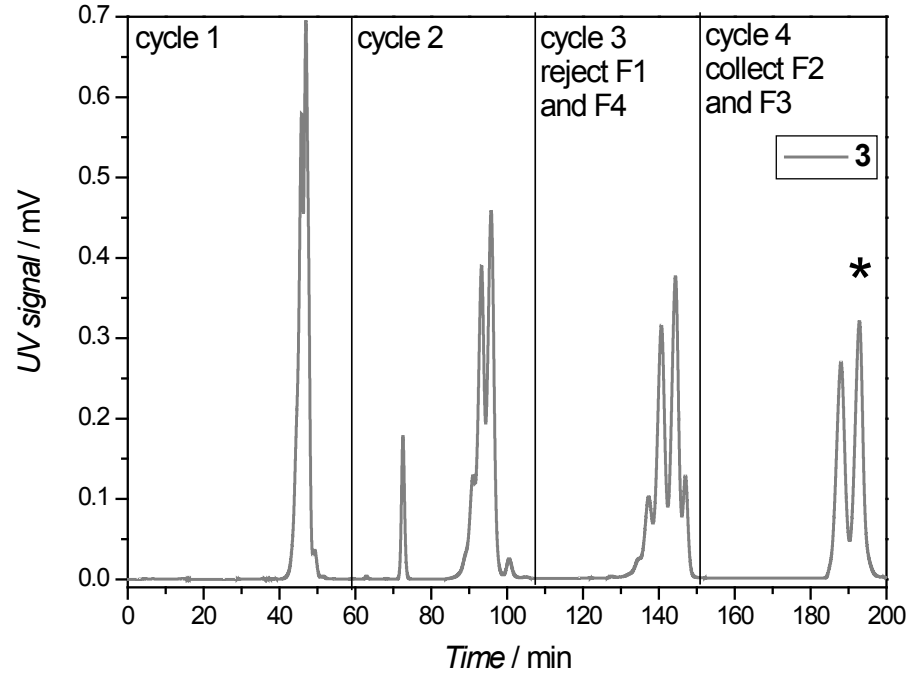

Figure S19. Recycling SEC trace recorded during consecutive purification cycles of *n*BuA-EHA-*t*BuA RAFT agent **3**. The desired oligomer is marked with an asterisk in all figures.

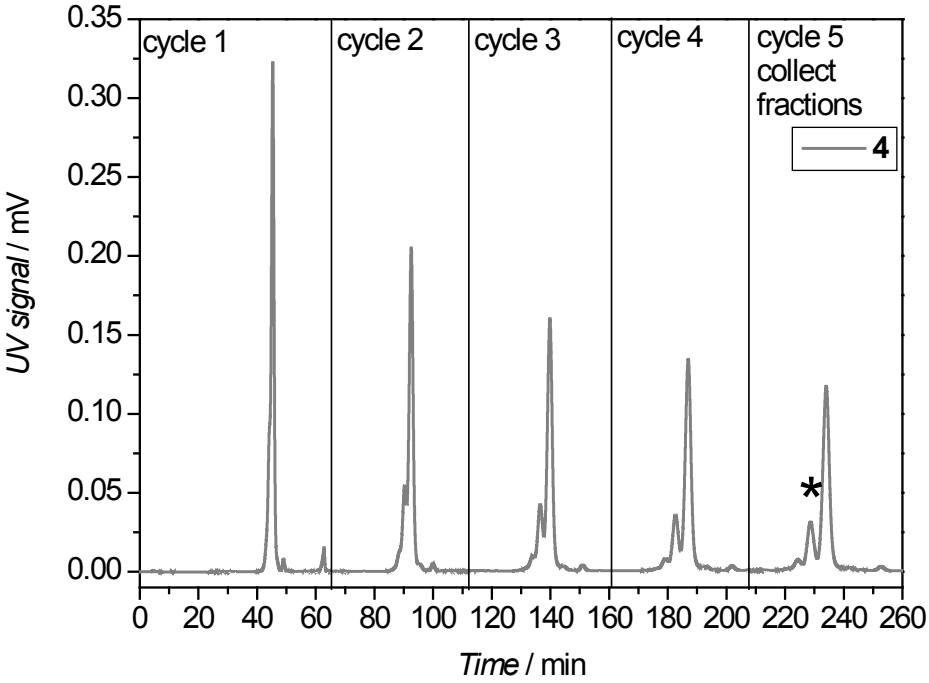

Figure S20. Recycling SEC trace recorded during consecutive purification cycles of *n*BuA-EHA-*t*BuA-*n*BuA RAFT agent **4**.

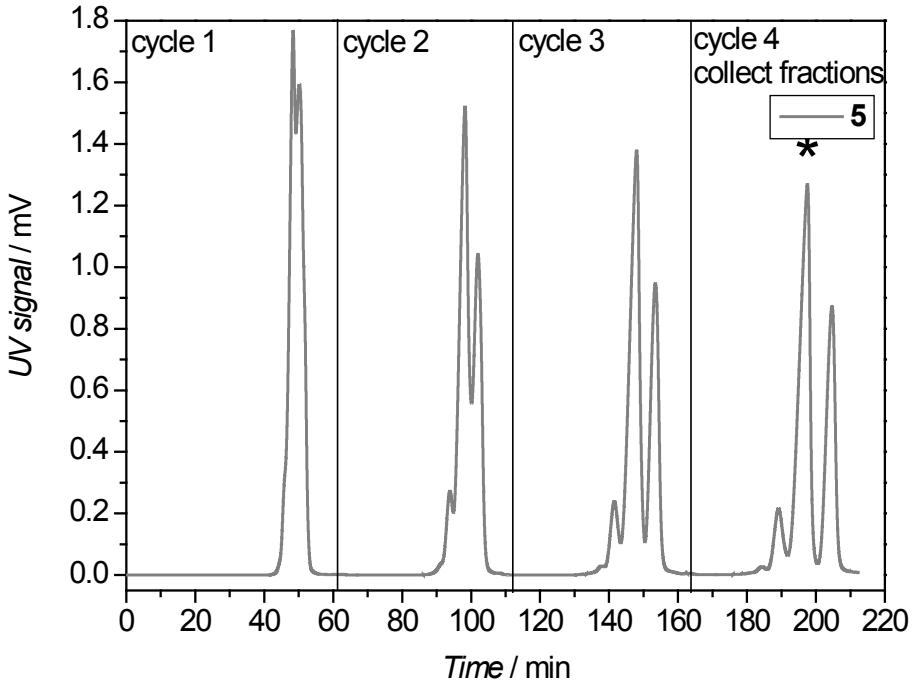

Figure S21. Recycling SEC trace recorded during consecutive purification cycles of *n*BuA-*t*BuA RAFT agent **5**.

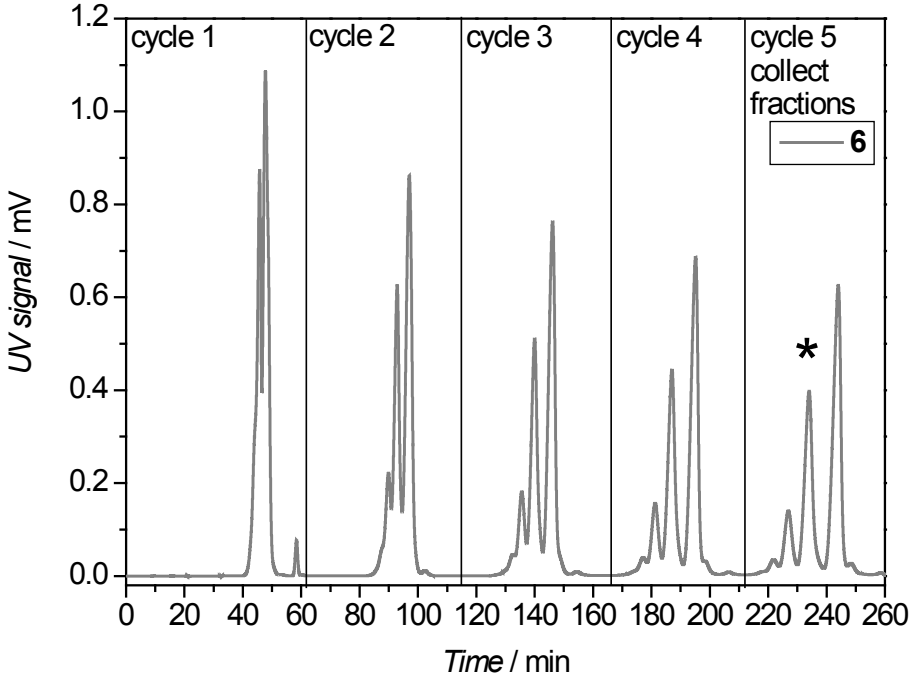

Figure S22. Recycling SEC trace recorded during consecutive purification cycles of *n*BuA-*t*BuA-EHA RAFT agent **6**.

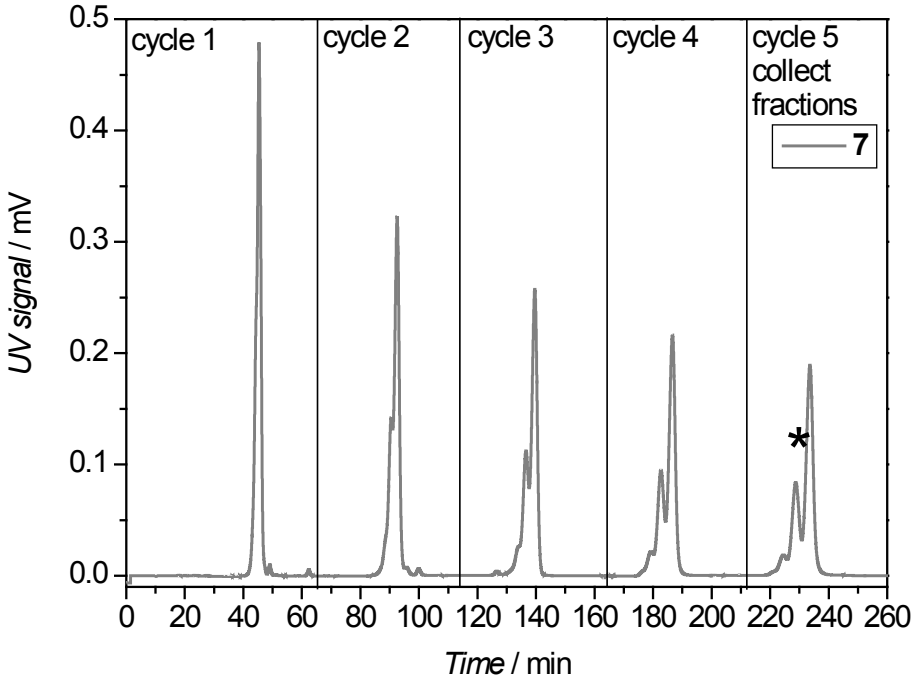

Figure S23. Recycling SEC trace recorded during consecutive purification cycles of *n*BuA-*t*BuA-EHA-*t*BuA RAFT agent **7**.

oligo-RAFT agent	Polymerization Time (min)	Crude Product Yield (%)	Purification Time (min)	Pure Product Yield (%)
1	10	≥ 90	110	55
2	10	≥ 90	210	46
3	10	≥ 90	200	20
4	10	≥ 90	240	4
5	10	≥ 90	210	50
6	10	≥ 90	250	20
7	10	≥ 90	240	12

Table S24. Overview of duration of polymerization as well as GPC purification and final yields for all oligo-RAFT agents.