Supporting Information

Streamlined synthesis of PEG-polypeptides directly from amino acids

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1. Materials and methods

1.1 Materials

All chemicals were purchased from MilliporeSigma (St. Louis, MO, USA) unless otherwise specified. Amino acids were purchased from Chem-Impex International, Inc. (Wood Dale, IL, USA). Methoxy poly(ethylene glycol) amine (mPEG-NH_2, M_n = 5 kDa, DP = 113) was purchased from Laysan Bio, Inc. (Arab, AL, USA). Anhydrous *N*,*N*-dimethylformamide (DMF) was treated with polymer-bound isocyanates (MilliporeSigma, St. Louis, MO, USA) to remove any amine residues and was stored at -40 ℃ in a glovebox. Tetrahydrofuran (THF) was treated with anhydrous sodium sulfate and was stored at room temperature. Anhydrous dichloromethane (DCM) and deuterated chloroform ($CDCl_3$) was treated with 3 Å molecular sieves and was stored at -40 ℃ in a glovebox. γ-Benzyl-L-glutamate *N*-carboxyanhydride (BLG-NCA),[1] N_ε-carboxybenzyl-L-lysine NCA (ZLL-NCA),[2] γ-(4-propargyloxybenzyl)-L-glutamate NCA (POB-NCA)[3], L-leucine NCA (Leu-NCA)[4] and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl-L-cysteine NCA (α-glc-C-NCA)[5] were synthesized according to the literature procedures without further purification. Specifically, α-glc-C-NCA was prepared from crude *N*-carbobenzyloxy-L-cysteine-1-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside) (Z-α-glc-C), which was simply purified by flush column and still contained acetic acid during column purification. Aqueous buffer (pH 3 and pH 7) containing boric acid, citric acid, and sodium phosphate (BCP buffer) were prepared according to the reported method.[6] Methoxy poly(ethylene glycol)-*b*-poly(γ-benzyl-L-glutamate) (PEG-PBLG) macroinitiator with terminal amine was synthesized by the reported method through mPEG-NH_2 mediated ring-opening polymerization of BLG-NCA, dissolved in $CHCl_3$ (50 mg/mL) and stored at -40 ℃.[7] The HPLC-grade, non-anhydrous solvents used for polymerization were directly purchased from commercial source without further treatment unless otherwise specified.

1.2 Instrumentation

Proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained using a Varian UI500NB (500 MHz) or Carver-Bruker 500 (500 MHz) or VNS750NB (750 MHz) spectrometer in the NMR laboratory, University of Illinois. All references for chemical shifts were decided by the residual protons of deuterated solvents and reported in ppm. MestReNova (version 12.0.3,

Mestrelab Research, Escondido, CA, USA), provided by the NMR laboratory at University of Illinois, was used in the analysis of NMR data. All gel permeation chromatography (GPC) data were collected *via* an instrument equipped with an isocratic pump (1260 Infinity II, Agilent, Santa Clara, CA, USA), a multi-angle static light scattering (MALS) detector with the detection wavelength at 658 nm (DAWN HELEOS-II, Wyatt Technology, Santa Barbara, CA, USA), and a differential refractometer (dRI) detector (Optilab T-rEX, Wyatt Technology, Santa Barbara, CA, USA). Separations were performed by serially connected size exclusion columns (three PLgel MIXED-B columns, 10 μm, 7.5 × 300 mm, Agilent, Santa Clara, CA, USA) which were maintained at a temperature of 40 ℃ using DMF containing 0.1 M LiBr as the mobile phase at a flow rate of 0.7 mL/min. The MALS detector was calibrated using pure toluene and then was used for the determination of the absolute molecular weights (MWs). All sample solutions were filtered by a 0.45 μm PTFE filter before the injection. The MWs of polypeptides were determined based on the *d*n/*d*c value of each sample calculated offline by using the internal calibration system processed by the software ASTRA 7 (version 7.1.3.15, Wyatt Technology, Santa Barbara, CA, USA). Fourier transform infrared (FTIR) spectra were obtained using a Perkin Elmer 100 serial FTIR spectrophotometer (PerkinElmer, Santa Clara, CA, USA) which was calibrated with polystyrene film. Circular dichroism (CD) measurements were performed on a JASCO J-815 CD spectrometer (JASCO, Easton, MD, USA). High performance liquid chromatography (HPLC) characterizations were done by a system equipped with an isocratic pump (1260 Infinity II, Agilent, Santa Clara, CA, USA) and a detector with the detection wavelength of detection from 190 nm to 400 nm (DAWN HELEOS-II, Wyatt Technology, Santa Barbara, CA, USA). Liquid chromatography–mass spectrometry (LC/MS) results were obtained using a Waters Q-TOF Ultima ESI in the Mass Spectrometry Laboratory at University of Illinois. The o/w emulsion was performed by a probe sonicator (Fisherbrand, Model FB 705, Thermo Fisher Scientific, Waltham, MA, USA) with a settled programmed pulse (20 W, 20 s, with a pulse sequence of 1-s pulse on and 1-s pulse off).

2. Experimental Procedures

2.1 Impurities analysis by LC/MS

The impurities analysis for non-purified NCA synthesized *via* the Fuchs-Farthing method was

performed by the following procedure. L-Leucine (Leu, 0.1 g, 0.76 mmol) was mixed with THF (2 mL) mentioned above. Phosgene (15 wt. % in toluene, 0.82 mL, 1.14 mmol) was then added into the mixture. The obtained mixture was stirred at 50 ℃ for 2 h in a capped, but not inert-gas protected vial, followed by removal of the solvent *in vacuo*. The obtained solid was dissolved in $CHCl_3$ (2 mL) and then treated with BCP buffer (500 μL, pH = 3) to extract impurities. After the aqueous phase was removed, benzylamine (300 μL, 2.75 mmol) was added to the remaining solution. The complete consumption of NCA monomers was confirmed by FTIR spectroscopy 5 min after the addition of benzylamine. Then the solution was treated with BCP buffer (500 μL, pH = 3) to extract extra benzylamine. The organic solution (10 μL) was diluted by water/acetonitrile solvent (990 μL, 1:1, v/v) and was then analyzed by LC/MS.

The analysis of impurities for non-purified NCA synthesized *via* the Leuchs method was performed *via* similar procedures. *N*-Benzyloxycarbonyl-L-leucine (0.1 g, 0.38 mmol) was dissolved in anhydrous DCM (4 mL). Dichloromethyl methyl ether (0.104 mL, 1.13 mmol) was then added into the *N*-benzyloxycarbonyl-L-leucine DCM solution. The mixture was stirred at 50 ℃ for 36 h. The solvent was later removed *in vacuo*. The rest of the procedures towards the analysis of impurities were same as those described in the previous paragraph for the studies of the impurities from the Fuchs-Farthing method.

2.2 Streamlined synthesis of PEG-polypeptides *via* Fuchs-Farthing method

γ-Benzyl-L-glutamate (BLG, 0.1 g, 0.42 mmol) was mixed with THF (2 mL) mentioned above. Phosgene (15 wt. % in toluene, 0.39 mL, 0.55 mmol) was then added into the mixture. The mixture was stirred at 50 ℃ for 2 h in a capped, but not inert-gas protected vial, followed by removal of the solvent *in vacuo*. The obtained solid was dissolved in regular $CHCl_3$ (2.1 mL) and washed with BCP buffer (570 μL, pH = 3). A $CHCl_3$ solution of *n*-hexylamine (200 mM, 1 μL) was then added to the NCA mixture, and the mixture was then vortexed for 30 s. The emulsion containing PEG-PBLG (206 μL, 1 mM PEG-PBLG, water/$CHCl_3$ = 1/50, m/m) was added into NCA/*n*-hexylamine solution followed by addition of BCP buffer (53 μL, pH = 7). Final condition: $[M]_0$ = 100 mM, [AS] = 0.5 mM, $[I]_0$ = 0.5 mM, water/$CHCl_3$ = 1/10, m/m.

After the polymerization was complete in ~ 15-30 min (monitored by FTIR), centrifugation was applied to promote phase separation to enable removal of the aqueous phase. The resulting polymers were purified by precipitation in hexane:ether (1:1, v/v), dried *in vacuo*, and analyzed by GPC. The isolated yield was calculated based on the mass of starting amino acids, assuming quantitative conversion during the phosgenation step.

2.3 Kinetic study of non-purified BLG-NCA initiated by PEG-PBLG in a w/o emulsion system in the presence of AS.

The BLG-NCA preparation and polymerization setup were same as those described above for the synthesis of PEG-polypeptide *via* Fuchs-Farthing method. $CDCl_3$ instead of $CHCl_3$ was used as solvent for polymerization. The conversion of BLG-NCA was monitored by NMR according to the literature procedures.[8] Final condition: $[BLG\text{-}NCA]_0$ = 0.075 M, [*n*-hexylamine]$_0$ = 0.375 mM, $[PEG\text{-}PBLG]_0$ = 0.5 mM, water/$CDCl_3$ = 1/10, m/m.

2.4 MWs of growing PEG-polypeptides

The BLG-NCA preparation and polymerization setup were same as those described above for the synthesis of PEG-polypeptide *via* Fuchs-Farthing method.

Several batches of PEG-polypeptides streamlined synthesis was set up following the procedures mentioned above. Final condition: $[BLG\text{-}NCA]_0$ = 0.075 M, [*n*-hexylamine]$_0$ = 0.375 mM, $[PEG\text{-}PBLG]_0$ = 0.5 mM, water/$CHCl_3$ = 1/10, m/m.

At selected time during the polymerization of the non-purified BLG-NCA, the obtained emulsion system (26 μL, 20 μL $CHCl_3$ and 6 μL BCP buffer presumably) was diluted by water/acetonitrile solvent (974 μL, 1:1, v/v) and was placed for 24 h before analyzed by LC/MS for the conversion of BLG-NCA. The polymerization system was quenched by trifluoroacetic acid (TFA) at the same time and was then poured into hexane/ether (40 mL, 1:1, v/v). The obtained solid was dried *in vacuo* and analyzed by GPC.

3. Supporting figures and tables

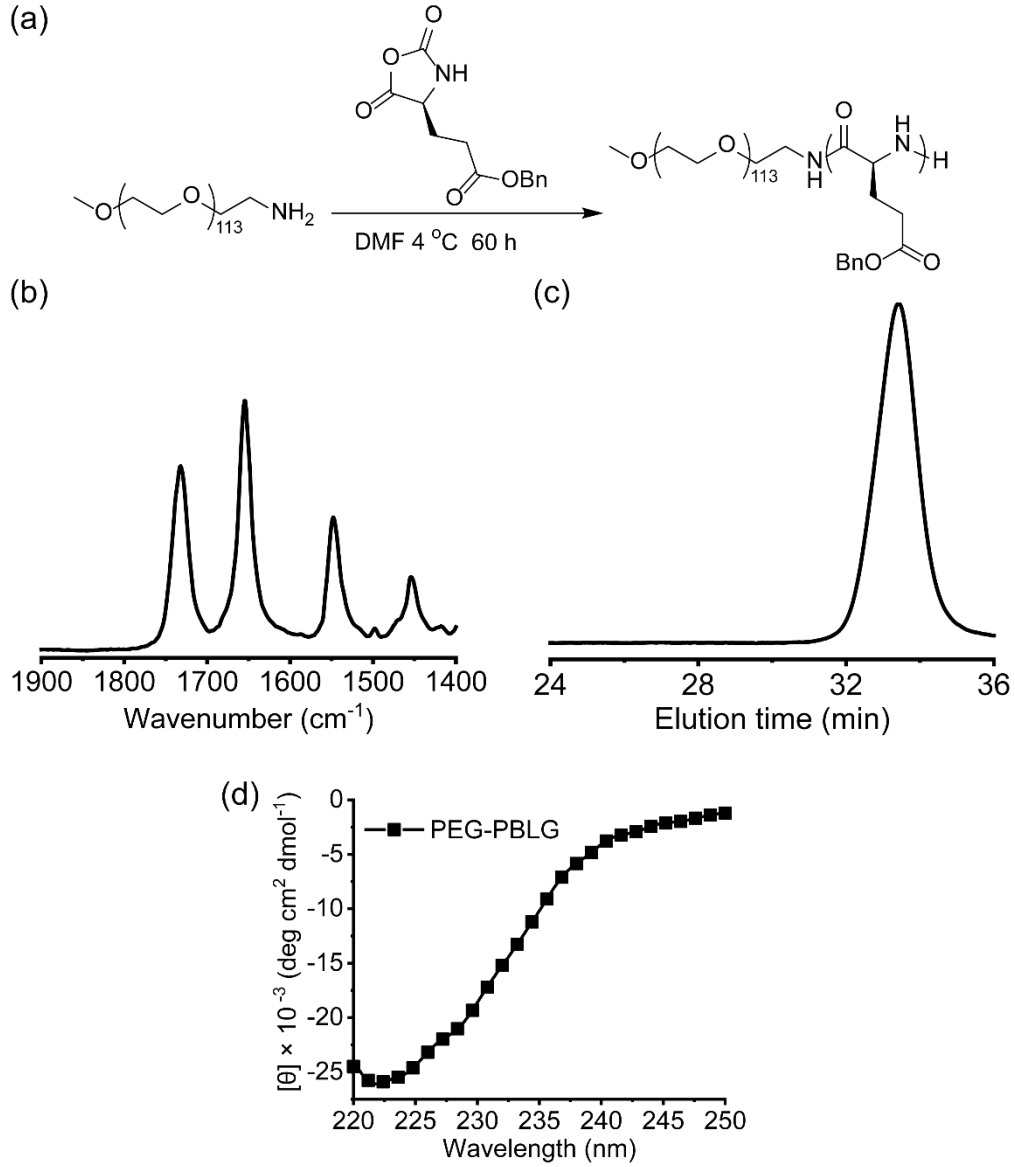

Figure S1. Characterization of PEG-PBLG macroinitiator. (a) Synthetic route to PEG-PBLG. (b) Solid state FTIR spectrum of PEG-PBLG. (c) Normalized GPC-LS trace of PEG-PBLG (M_n = 14.5 kDa, $Đ$ = 1.1, DP for PBLG = 43). (d) CD spectrum of PEG-PBLG in DCM.

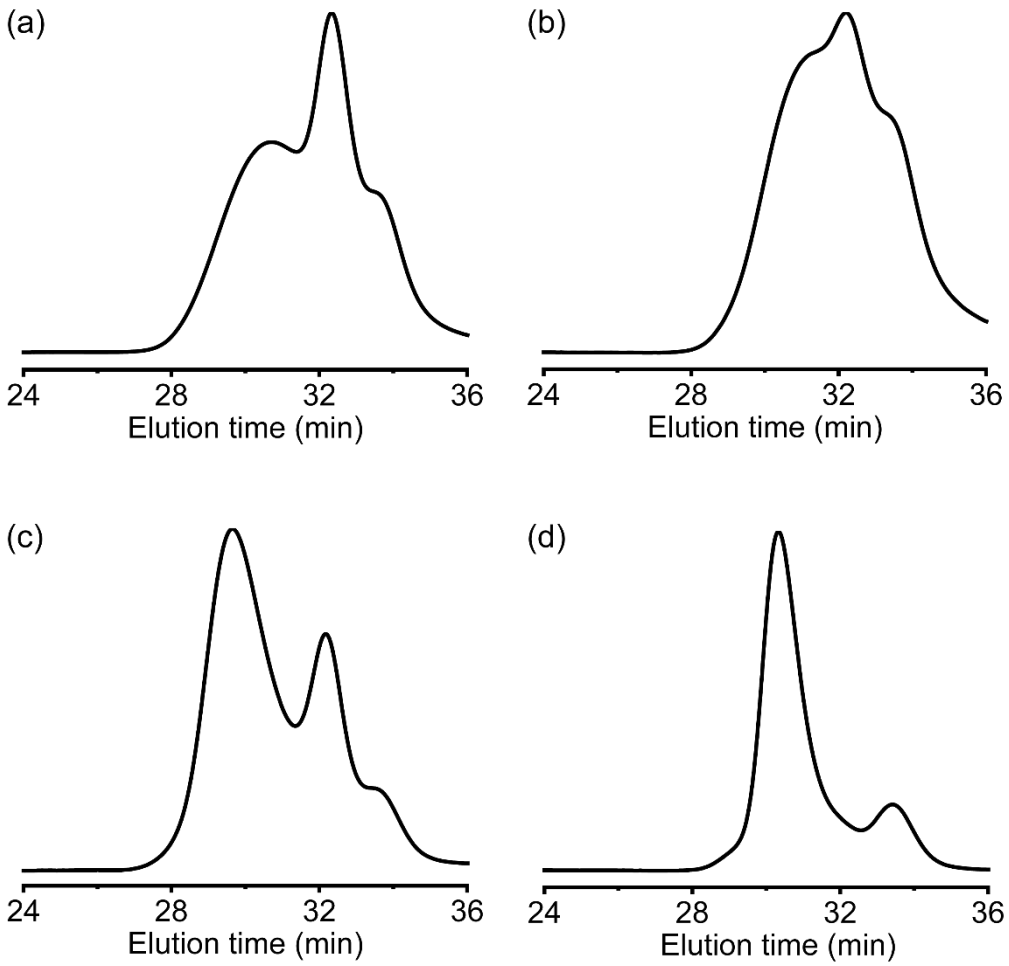

Figure S2. GPC analysis (dRI signal) for polypeptides directly synthesized from various non-purified NCAs using SIMPLE polymerization initiated by PEG-PBLG in the absence of AS. $[I]_0$ = 0.5 mM. Polypeptides synthesized from: (a) non-purified BLG-NCA, $[M]_0$:$[I]_0$ = 100:1; (b) non-purified BLG-NCA, $[M]_0$:$[I]_0$ = 200:1; (c) non-purified ZLL-NCA, $[M]_0$:$[I]_0$ = 100:1; (d) non-purified POB-NCA, $[M]_0$:$[I]_0$ = 100:1.

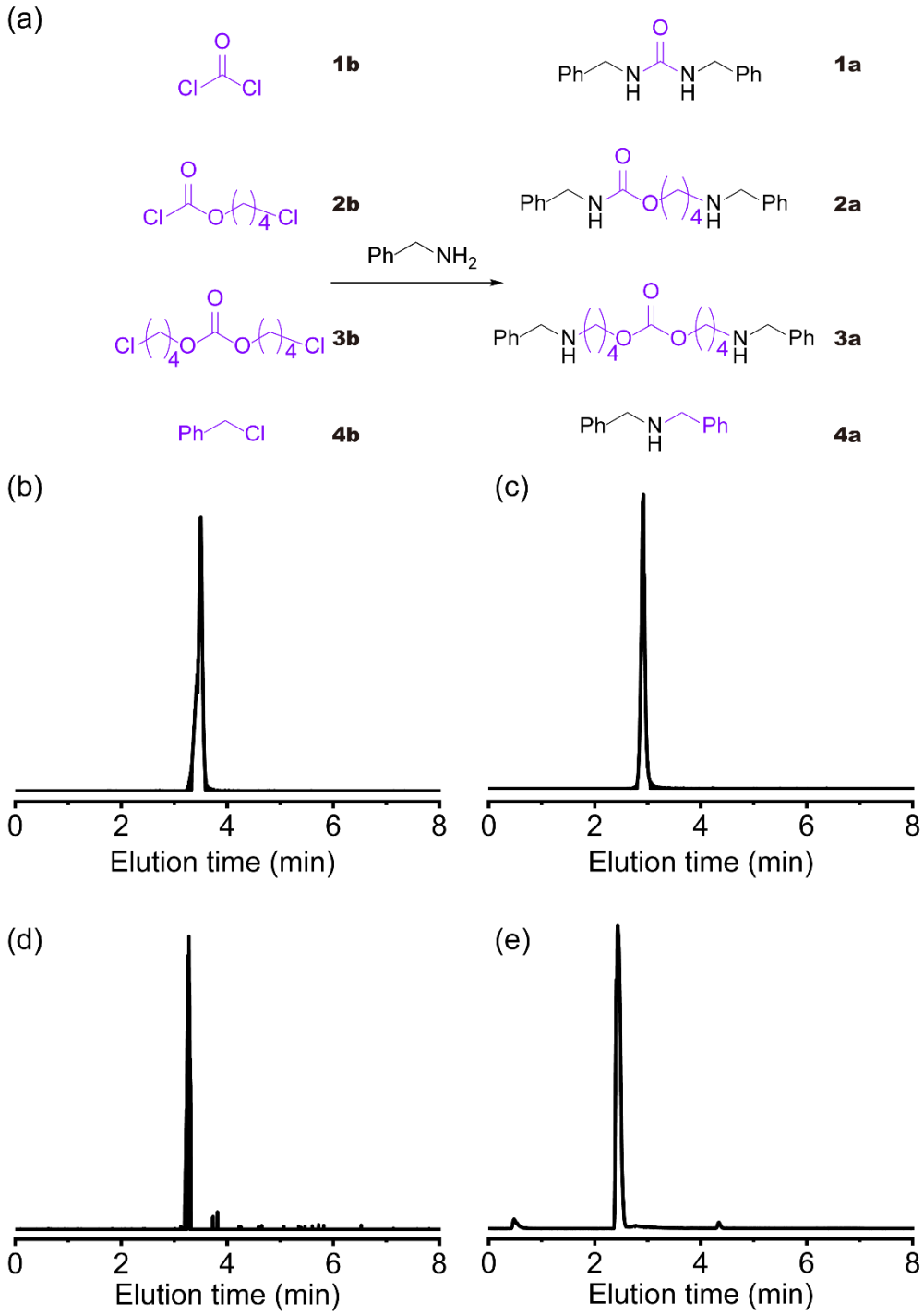

Figure S3. Impurities analysis for the reaction of benzylamine and the non-purified Leu-NCA derived from its reaction with phosgene. (a) Chemical structures for observed compounds **1a**, **2a**, **3a**, **4a** and the structures for impurities **1b**, **2b**, **3b** and **4b** in Leu-NCA. (b, c, d, e) Trace maps for the observed compounds in LC-MS: (b) **1a**, (c) **2a**, (d) **3a**, and (e) **4a**. The maximum deviation between obtained *m/z* and expected *m/z* is 0.001.

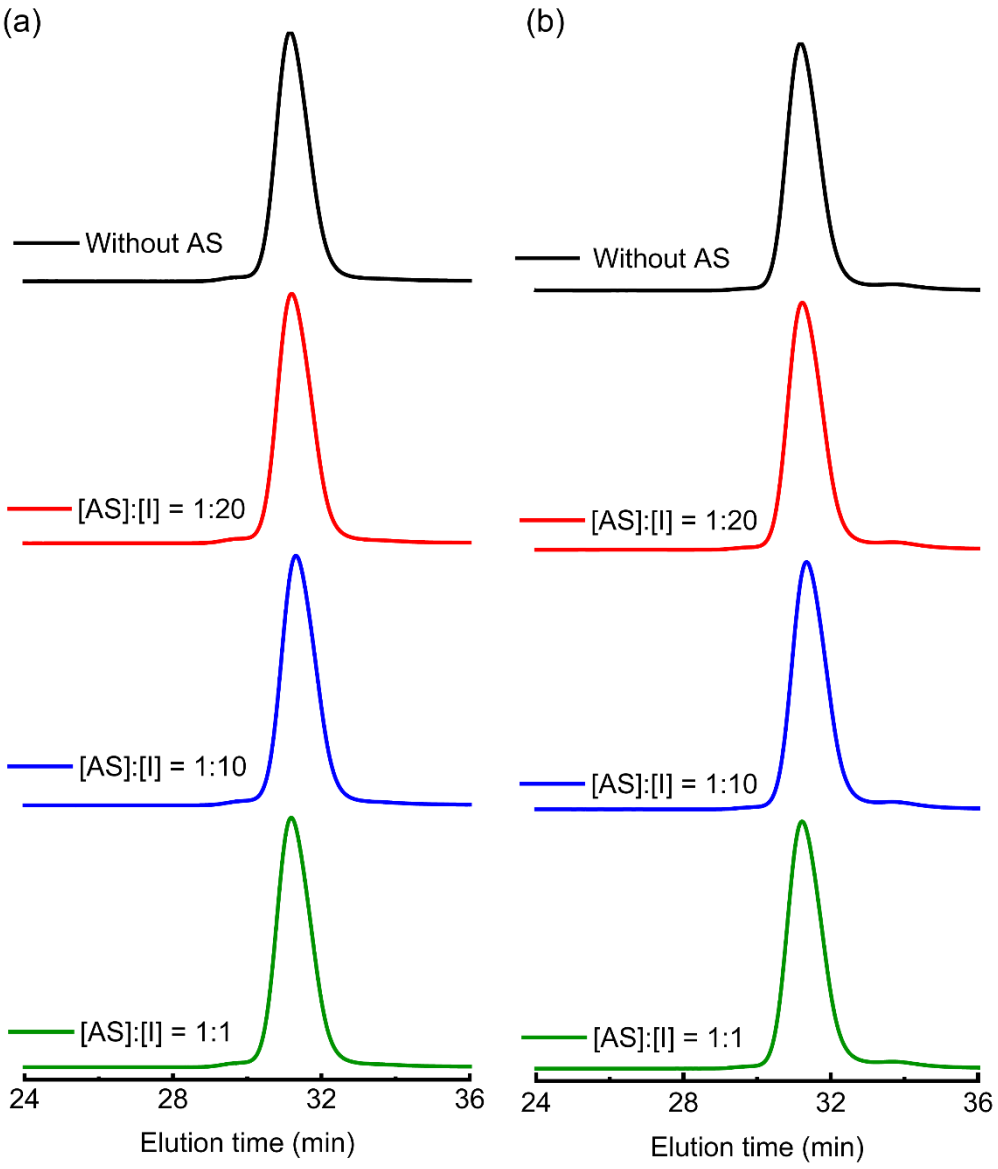

Figure S4. GPC analysis of polypeptides from purified BLG-NCA with different amounts of *n*-hexylamine as AS: (a) LS traces. (b) dRI traces. $[M]_0$ = 0.1 M, $[M]_0/[I]_0$ = 200.

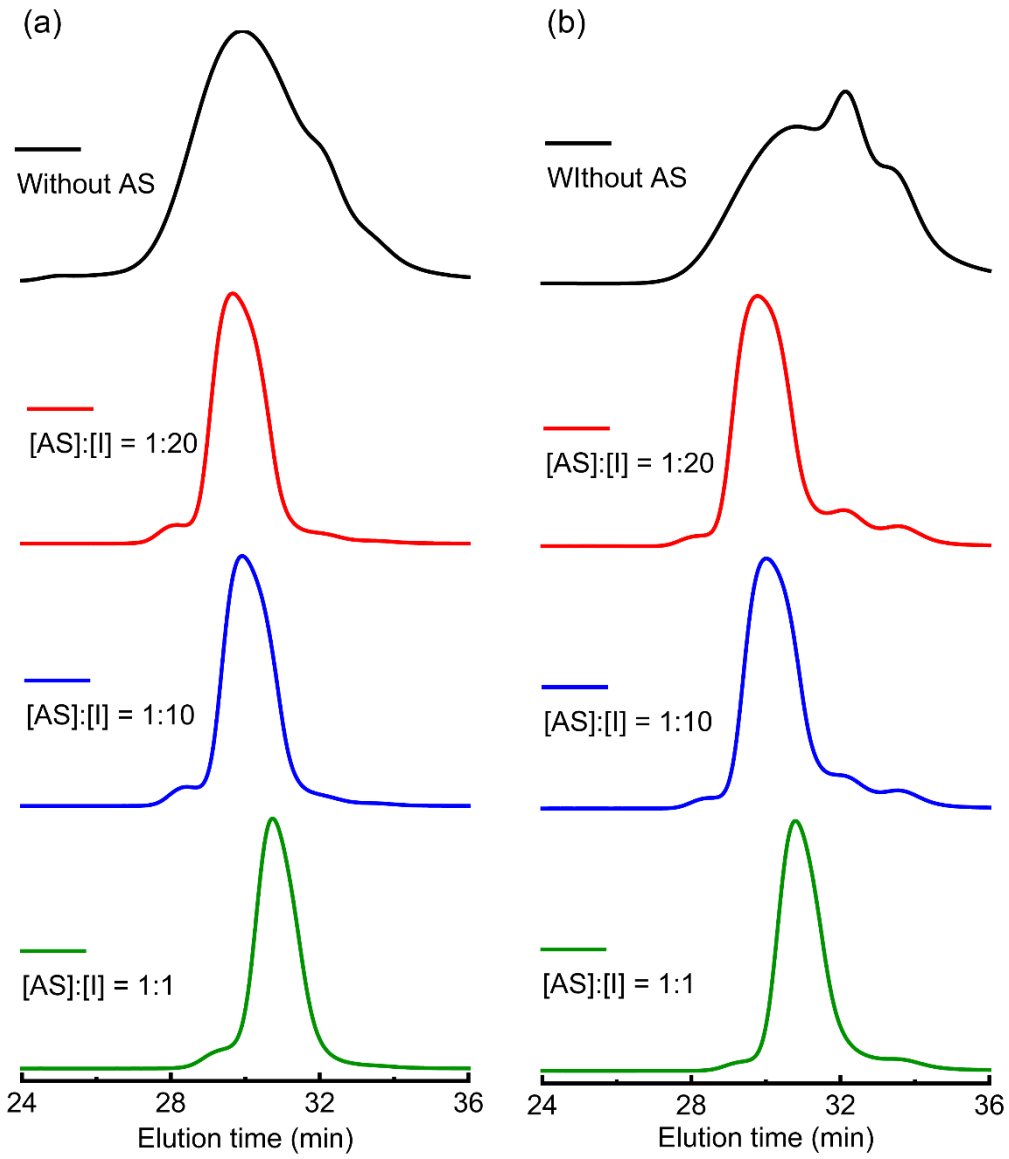

Figure S5. GPC analysis of polypeptides prepared from SIMPLE polymerization of non-purified BLG-NCA derived from Fuchs-Farthing method with different amounts of *n*-hexylamine as AS: (a) LS traces. (b) dRI traces. $[M]_0$ = 0.1 M, $[M]_0/[I]_0$ = 200.

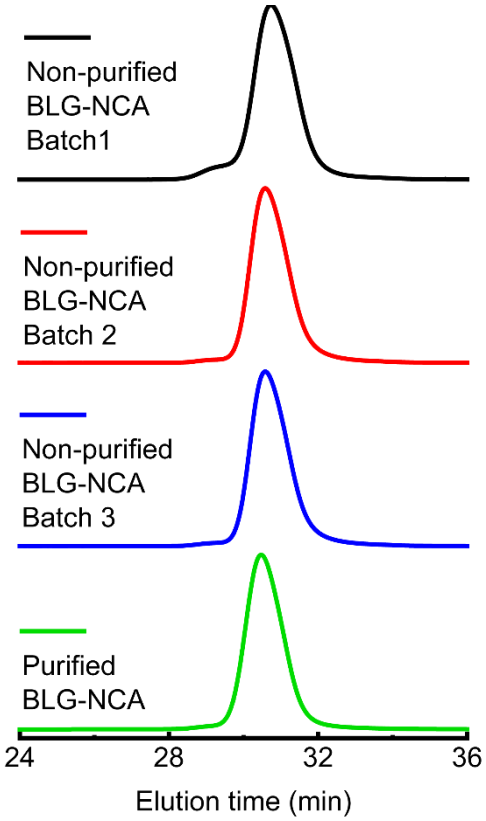

Figure S6. GPC analysis (LS traces) of polypeptides from the polymerization of three different batches of non-purified BLG-NCA and one batch of purified BLG-NCA initiated from different batches of macroinitiators using *n*-hexylamine as AS. $[M]_0$ = 0.1 M, $[AS]_0$ = 0.5 mM, $[M]_0/[I]_0$ = 200.

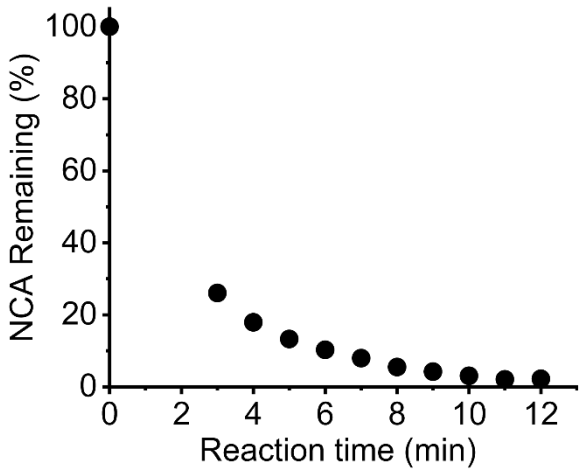

Figure S7. Kinetic study of non-purified BLG-NCA initiated by PEG-PBLG in a w/o emulsion system using *n*-hexylamine as AS. The polymerization was monitored by ^{1}H-NMR in $CDCl_3$. $[M]_0$ = 0.075 M, $[AS]_0$ = 0.375 mM, $[M]_0/[I]_0$ = 150.

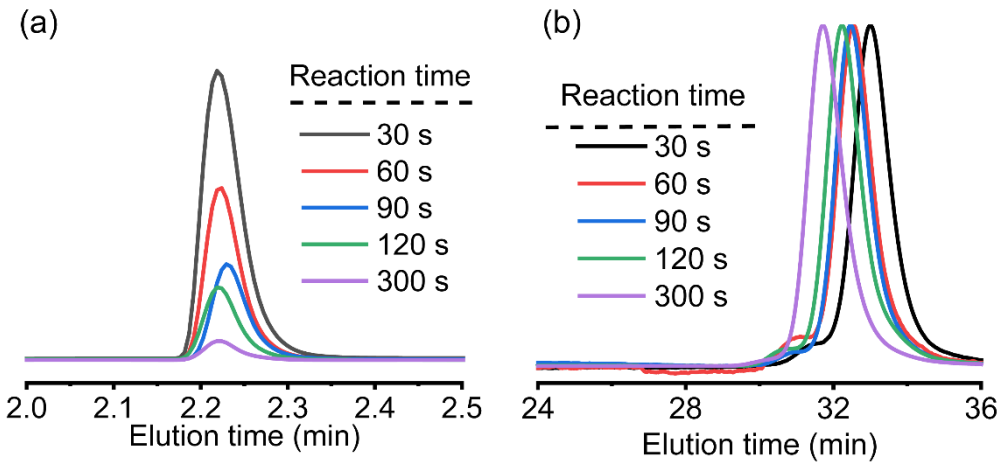

Figure S8. (a) HPLC analysis for BLG-NCA concentration at different polymerization time in the presence of *n*-hexylamine as AS by detecting the signal for their products of hydrolysis. (b) GPC analysis (LS traces) for polypeptides quenched at different polymerization time. $[M]_0$ = 0.075 M, $[AS]_0$ = 0.375 mM, $[M]_0/[I]_0$ = 150.

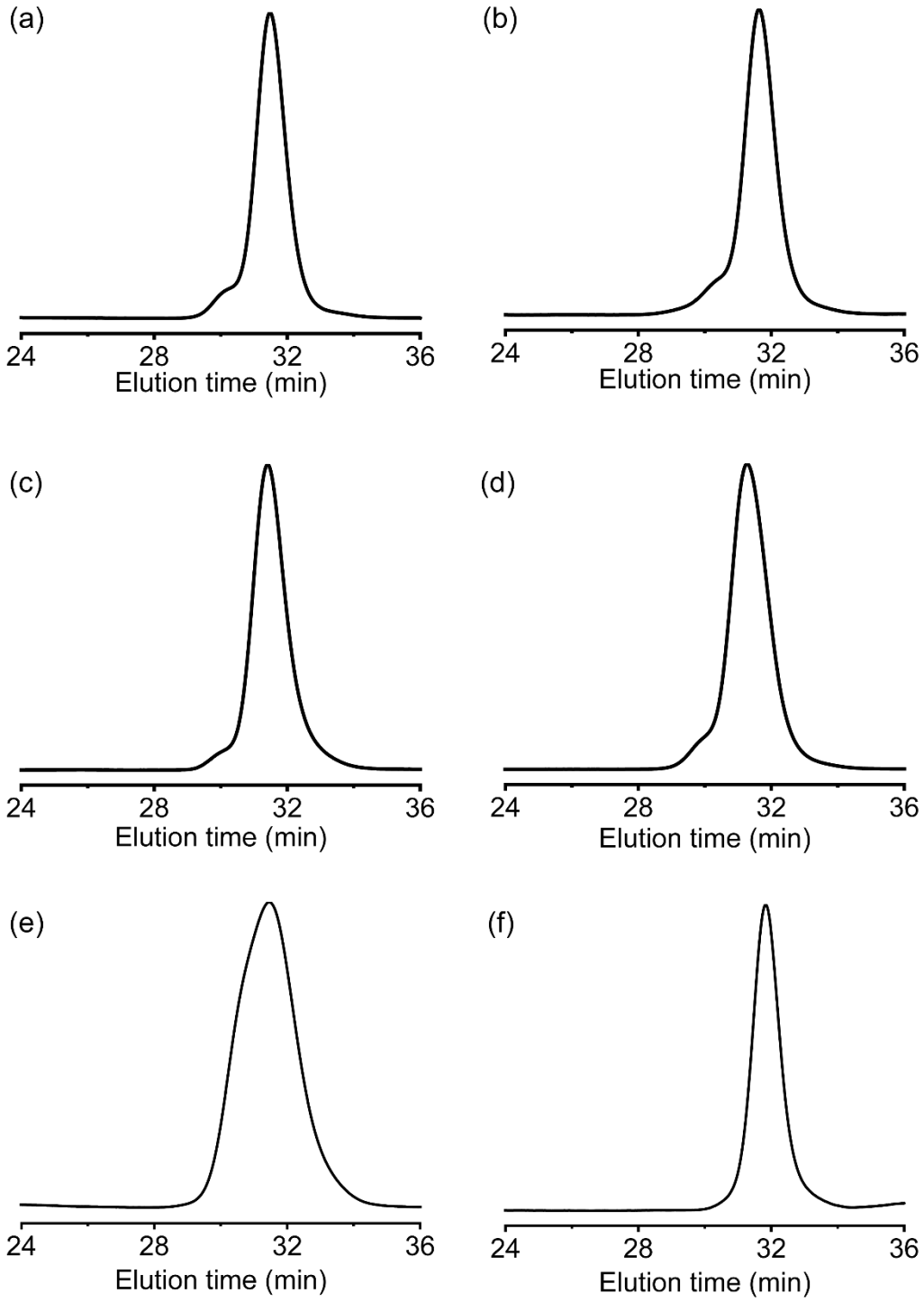

Figure S9. GPC analysis (LS traces) for polypeptides prepared *via* streamlined synthesis in the presence of *n*-hexylamine as AS. (a) $PZLL_{100}$, (b) $PPOB_{100}$, (c) random co-polypeptides with $PBLG_{40}$-*r*-$PZLL_{40}$-*r*-$Pleu_{20}$, and (d) random co-polypeptides with $PPOB_{80}$-*r*-$Pleu_{20}$, (e) random co-polypeptides with $PBLG_{75}$-*r*-$PBLS_{25}$, (e) $P(\alpha\text{-glc-C})_{100}$.

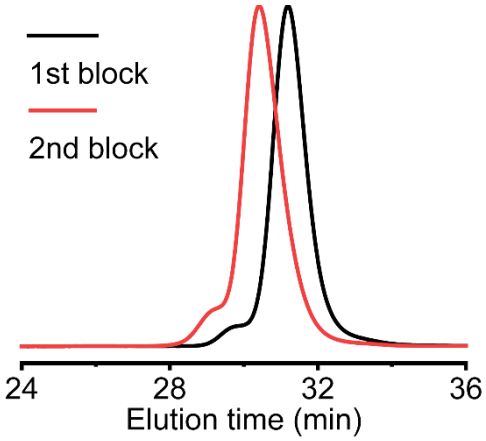

Figure S10. GPC analysis (LS traces) for block co-polypeptides prepared from streamlined synthesis in the presence of *n*-hexylamine as AS. Black line: first block PBLG$_{50}$-*r*-PZLL$_{50}$; Red line: second block PPOB$_{50}$. $[M]_0/[I]_0$ = 100 for first block and $[M]_0/[I]_0$ = 50 for second block.

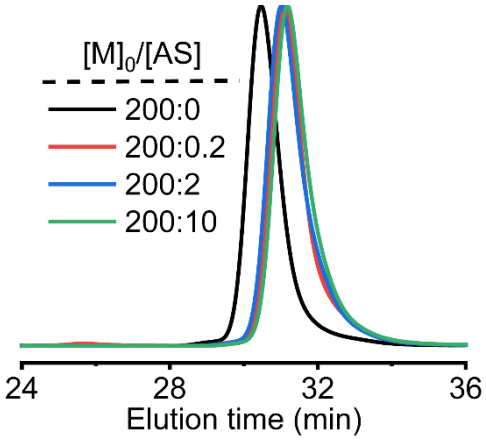

Figure S11. GPC analysis (LS traces) of polypeptide from non-purified BLG-NCA synthesized from Leuchs method for the test on the effect of *n*-hexylamine as AS. $[M]_0/[I]_0 = 200$.

Table S1. Summary of the synthesis of polypeptides from various non-purified NCAs without the addition of AS[a]

Entry	NCAs	$[M]_0/[I]_0$	M_n[b]/M_n*[c] (kDa)	$Đ$[b]
1	BLG-NCA	100	35.2/37.0	1.63
2	BLG-NCA	200	37.1/58.8	1.47
3	ZLL-NCA	100	56.4/41.2	1.94
4	POB-NCA	100	52.1/41.8	1.73

[a]The polymerization was carried out at room temperature using PEG-PBLG initiator. The conversion of NCA intermediate was above 99% as confirmed by FTIR. [b]Obtained by GPC. [c]Obtained MWs /Expected MWs*.

Table S2. Summary of the synthesis of polypeptides from purified BLG-NCA in the presence of different amounts of AS[a]

Entry	$[M]_0$:$[AS]_0$:$[I]_0$	M_n[b]/M_n*[c] (kDa)	$Đ$[b]
1	200:0:1	54.6/58.8	1.05
2	200:0.05:1	51.6/58.8	1.05
3	200:0.1:1	49.2/58.8	1.06
4	200:1:1	52.7/58.8	1.05

[a]BLG-NCA was prepared from Fuchs-Farthing method and purified by three times recrystallization. The polymerization was carried out at room temperature using PEG-PBLG initiator in the presence of different amounts of *n*-hexylamine as AS. The conversion of NCA intermediate was above 99% as confirmed by FTIR. [b]Obtained by GPC. [c]Obtained MWs/Expected MWs*.

Table S3. Summary of the synthesis of polypeptides from non-purified BLG-NCA in the presence of different amounts of AS[a]

Entry	$[M]_0$:$[AS]_0$:$[I]_0$	M_n/M_n*[c,d] (kDa)	$Đ$[c]
1[b]	200:0:1	54.6/58.8	1.05
2	200:0:1	41.5/58.8	1.66
3	200:0.05:1	71.5/58.8	1.44
4	200:0.1:1	63.6/58.8	1.36
5	200:1:1	53.0/58.8	1.16

[a]The non-purified BLG-NCA was prepared from Fuchs-Farthing method and was used after the removal of solvent and aqueous extraction. The polymerization was carried out at room temperature using PEG-PBLG initiator in the presence of different amounts of *n*-hexylamine as AS. The conversion of NCA intermediate was above 99% as confirmed by FTIR. [b]Data from **Table S3** entry 1 as reference where polypeptides synthesized from purified BLG-NCA presented expected MWs and narrow dispersity. [c]Obtained by GPC. [d]Obtained MWs /Expected MWs*.

Table S4. Summary of the synthesis of polypeptides from different batches of non-purified BLG-NCA or purified BLG-NCA in the presence of AS[a]

Entry	Batch	$[M]_0$:$[AS]_0$:$[I]_0$	M_n/M_n*[c,d] (kDa)	$Đ$[c]
1	1	200:1:1	53.0/58.8	1.16
2	2	200:1:1	59.1/58.8	1.10
3	3	200:1:1	58.5/58.8	1.08
4[b]	Purified BLG-NCA	200:1:1	58.3/58.8	1.05

[a]The non-purified BLG-NCA was prepared from Fuchs-Farthing method and was used after the removal of solvent and aqueous extraction. The polymerization was carried out at room temperature using PEG-PBLG initiator at the presence of *n*-hexylamine as AS. The conversion of NCA intermediate was above 99% as confirmed by FTIR. [b]Polypeptides from purified BLG-NCA as reference. [c]Obtained by GPC. [d]Obtained MWs /Expected MWs*.

Table S5. Summary of the synthetic polypeptides from non-purified BLG-NCA at different NCA conversion in the presence of AS[a]

Entry	Time (s)	[NCA][b] (μg/mL)	Conversion (%)	M_n[c]/M_n*[d] (kDa)	$Đ$[c]
1	30	136.1	31.3	24.6/25.2	1.06
2	60	107.6	45.6	30.2/29.9	1.06
3	90	59.0	70.2	35.8/38.0	1.08
4	120	44.4	77.6	39.5/40.4	1.10
5	300	10.4	94.7	46.5/46.0	1.10

[a]The polymerization was carried out at room temperature using PEG-PBLG initiator in the presence of *n*-hexylamine as AS. At different reaction time, the polymerization was quenched by adding water/acetonitrile solvent (for the characterization of NCA concentration) or by adding TFA (for the characterization of MWs) simultaneously. [b]Concentration calculated from products of hydrolysis by HPLC. $[NCA]_0$ = 198.11 μg/mL. [c]Obtained by GPC. [d]Obtained MWs /Expected MWs*. $[M]_0$ = 0.075 M, $[M]_0$:$[I]_0$ = 150:1.

Table S6. Summary of the polypeptides synthesized in large scale vs. in small scale[a]

Entry	Monomer	$[M]_0/[I]_0$	M_n/M_n*[d,e](kDa)	$Đ$[d]
1	BLG-NCA[b]	200	58.3/58.8	1.05
2	BLG[c]	200	60.5/58.8	1.07

[a]The polymerization was carried out at room temperature initiated by PEG-PBLG in the presence of *n*-hexylamine as AS. The conversion of NCA intermediate was above 99% as confirmed by FTIR. [b]BLG-NCA was prepared *via* Fuchs-Farthing method and purified *via* three times recrystallization. Polypeptides were synthesized in 10 mg scale. [c]Polypeptides were synthesized from non-purified BLG-NCA synthesized from Fuchs-Farthing method using 1 gram of BLG as starting materials. [d]Obtained by GPC. [e]Obtained MWs /Expected MWs*.

Table S7. Summary of the streamlined synthesis of PEG-polypeptides containing random co-polypeptides[a]

Entry	Composition	Expected Ratio[b]	Obtained Ratio in mixed NCAs[c]	Obtained ratio in polymer[d]
1	BLG$_{40}$-*r*-ZLL $_{40}$-*r*-Leu$_{20}$	40:40:20	40:41:19	37:41:22
2	POB$_{80}$-*r*-Leu$_{20}$	80:20	78:22	82:18
3	BLG$_{75}$-*r*-BLS$_{25}$	75:25	75:25	73:27

[a]The polymerization was carried out at room temperature using PEG-PBLG initiator in the presence of *n*-hexylamine as AS. The conversion of NCA intermediate was above 99% as confirmed by FTIR. Random co-polypeptides were prepare from the polymerization of non-purified NCA mixture synthesized from mixed amino acids. [b]Expected composition. [c]Obtained composition for freshly prepared NCAs mixture from ^{1}H NMR. [d]Obtained composition in obtained polypeptides from ^{1}H NMR.

Table S8. Summary of the streamlined synthesis of PEG-polypeptides containing block co-polypeptides[a]

Entry	Amino acid	$[M]_0/[I]_0$	M_n/M_n*[b,c] (kDa)	$Đ^b$
1	BLG	50	23.6/26.0	1.06
2	BLG, POB	50-*b*-50 [c]	39.5/39.6	1.10
3	BLG, POB, ZLL	50-*b*-50-*b*-50[c]	56.1/52.7	1.20
4	BLG, ZLL	50-*r*-50[d]	40.6/39.1	1.07
5	BLG, ZLL, POB	(50-*r*-50)-*b*-50 [c d]	52.6/52.7	1.15

[a]The polymerization was carried out at room temperature using PEG-PBLG initiator in the presence of *n*-hexylamine as AS. The conversion of NCA intermediate was above 99% as confirmed by FTIR. Block co-polypeptides were synthesized by adding freshly prepared NCAs sequentially. [b]Obtained by GPC. [c]Obtained MWs /Expected MWs*.

Table S9. Summary of the synthesis of polypeptides from non-purified BLG-NCA synthesized from Leuchs method in the presence of different amounts of AS[a]

Entry	$[M]_0$:$[AS]_0$:$[I]_0$	M_n/M_n*[b,c] (kDa)	$Đ$[b]
1	200:0:1	67.2/58.8	1.07
2	200:0.2:1	47.2/58.8	1.06
3	200:2:1	51.1/58.8	1.05
4	200:10:1	48.3/58.8	1.05

[a] Non-purified BLG-NCA was prepared from Leuchs method and was used after the removal of solvent and aqueous extraction. The polymerization was carried out at room temperature using PEG-PBLG initiator in the presence of different amounts of *n*-hexylamine as AS. The conversion of NCA intermediate was above 99% as confirmed by FTIR. [b]Obtained by GPC. [c]Obtained MWs/Expected MWs*.

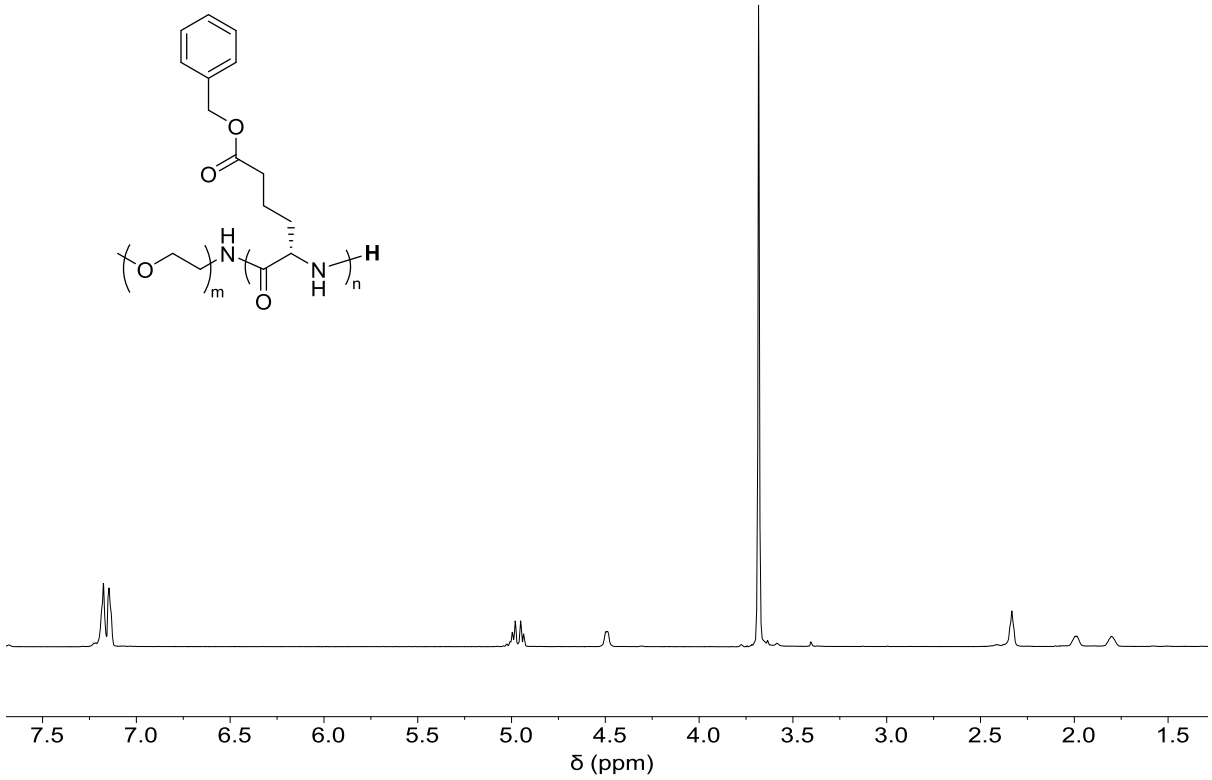

Figure S12. ^{1}H NMR spectrum (750 MHz) of PEG-PBLG macroinitiator in $CDCl_3$/TFA-*d* (85:15, v/v).

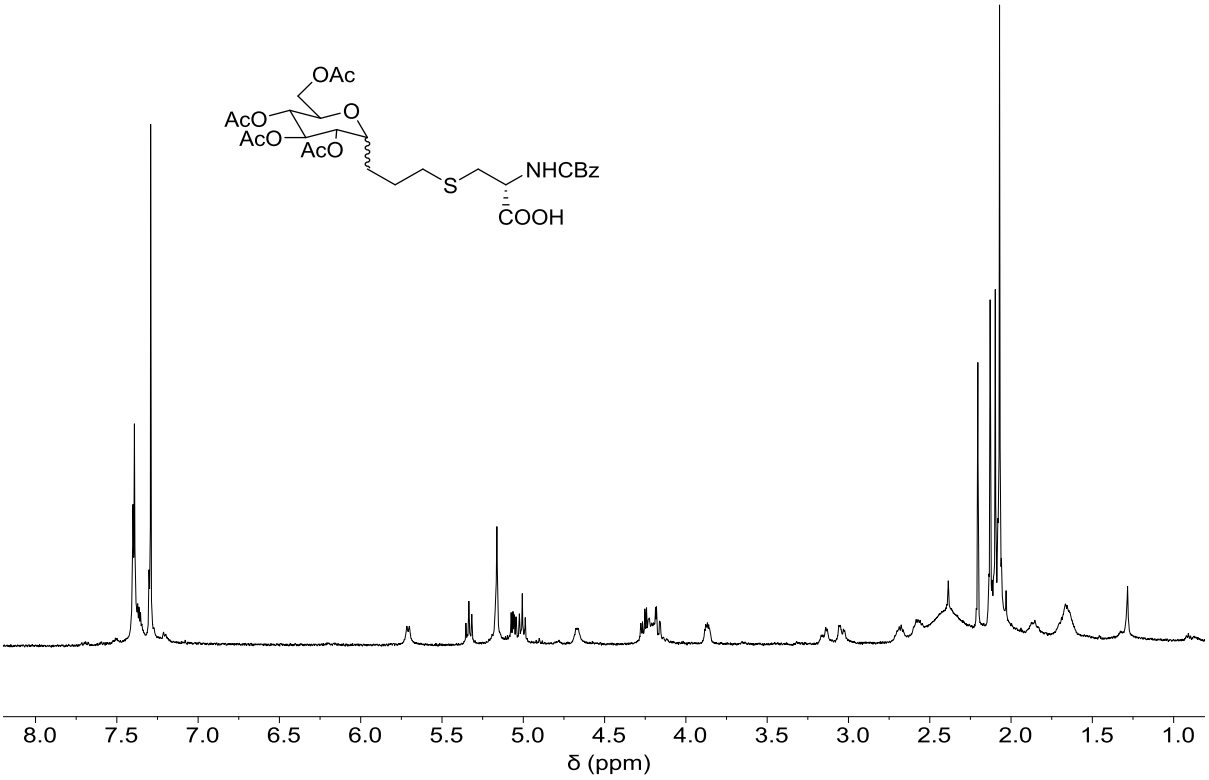

Figure S13. ^{1}H NMR spectrum (500 MHz) of crude Z-α-glc-C in $CDCl_3$.

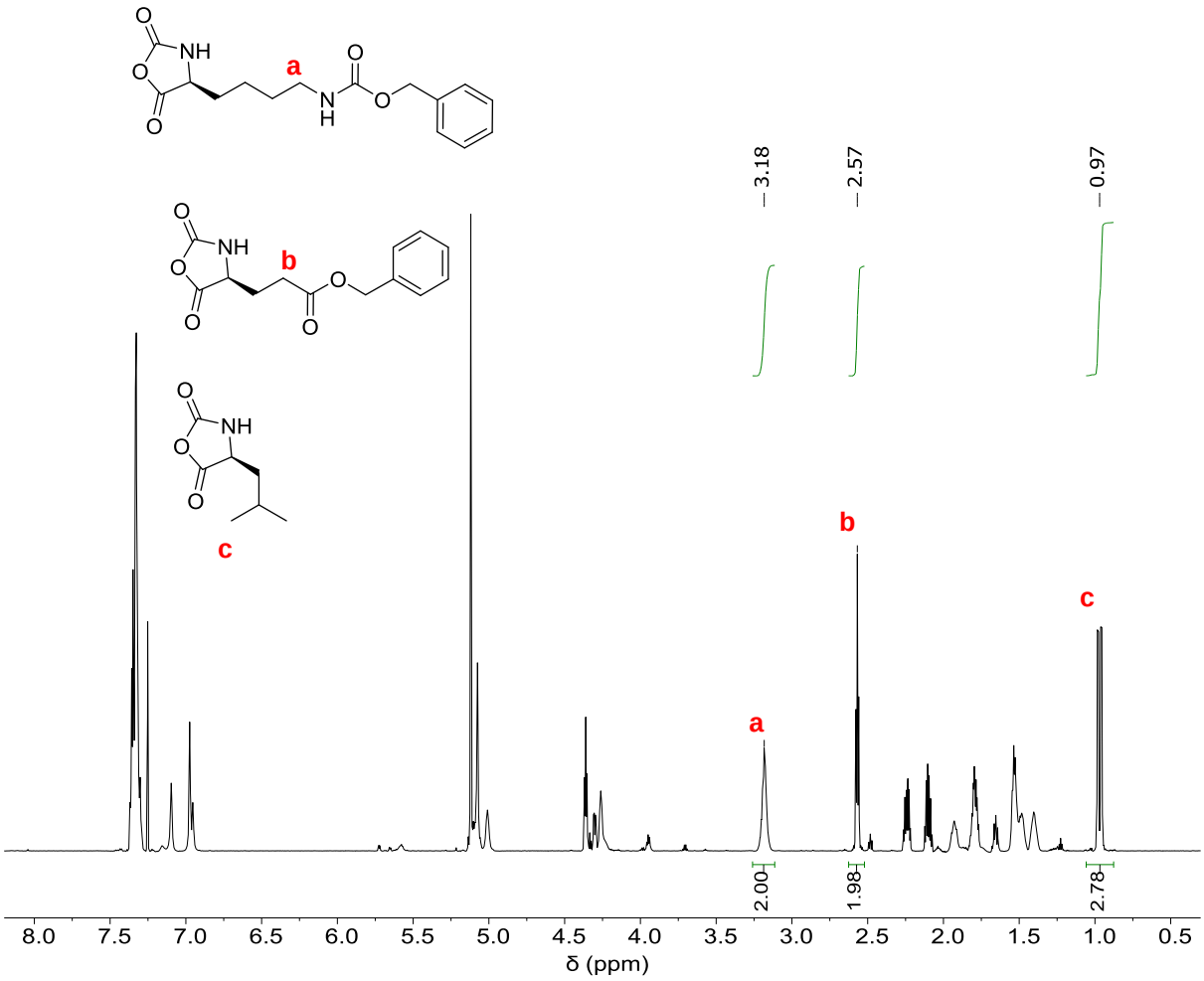

Figure S14. ^{1}H NMR spectrum (500 MHz) of mixture of non-purified BLG-NCA, ZLL-NCA and Leu-NCA (designed molar ratio 2:2:1) in $CDCl_3$ synthesized from Fuchs-Farthing method in one pot.

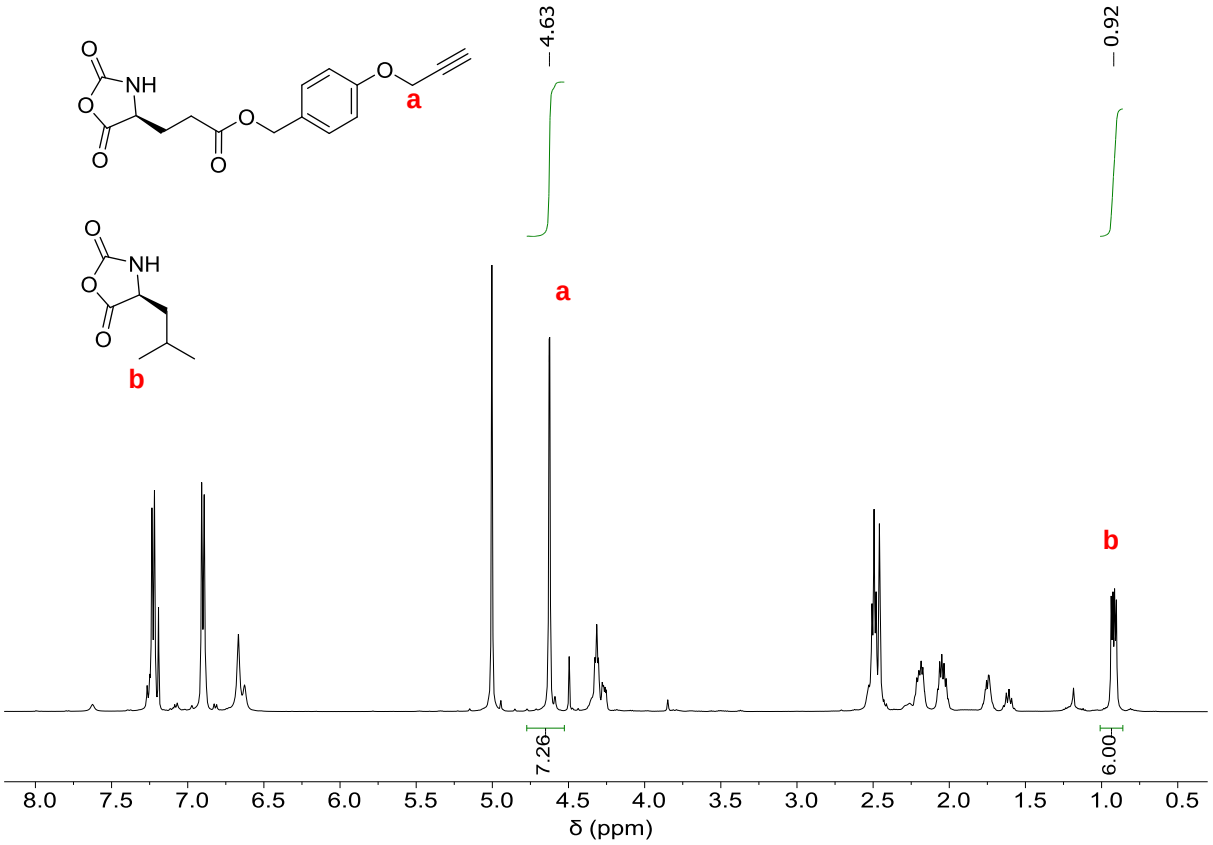

Figure S15. ^{1}H NMR spectrum (500 MHz) of non-purified POB-NCA and Leu-NCA (designed molar ratio 4:1) in $CDCl_3$ synthesized from Fuchs-Farthing method in one pot.

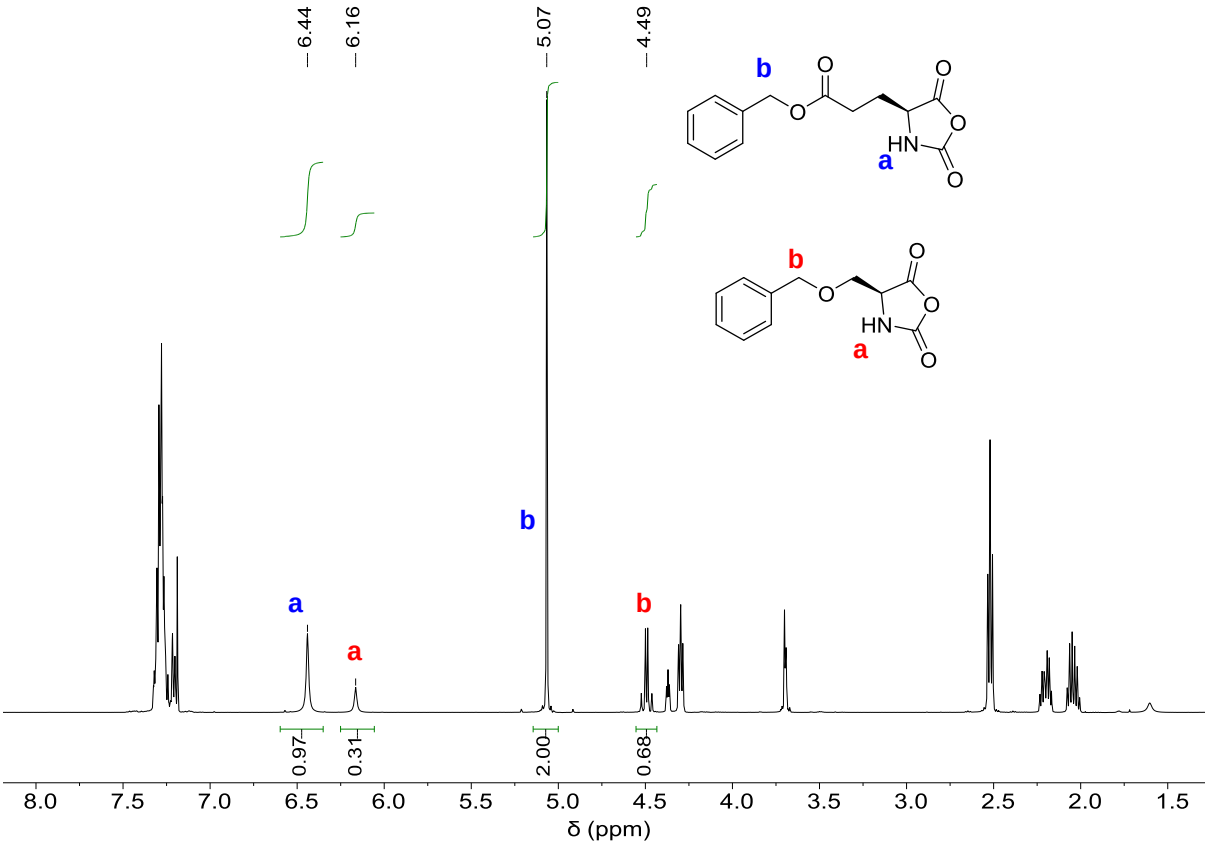

Figure S16. ^{1}H NMR spectrum (500 MHz) of non-purified BLG-NCA and BLS-NCA (designed molar ratio 3:1) in $CDCl_3$ synthesized from Fuchs-Farthing method in one pot.

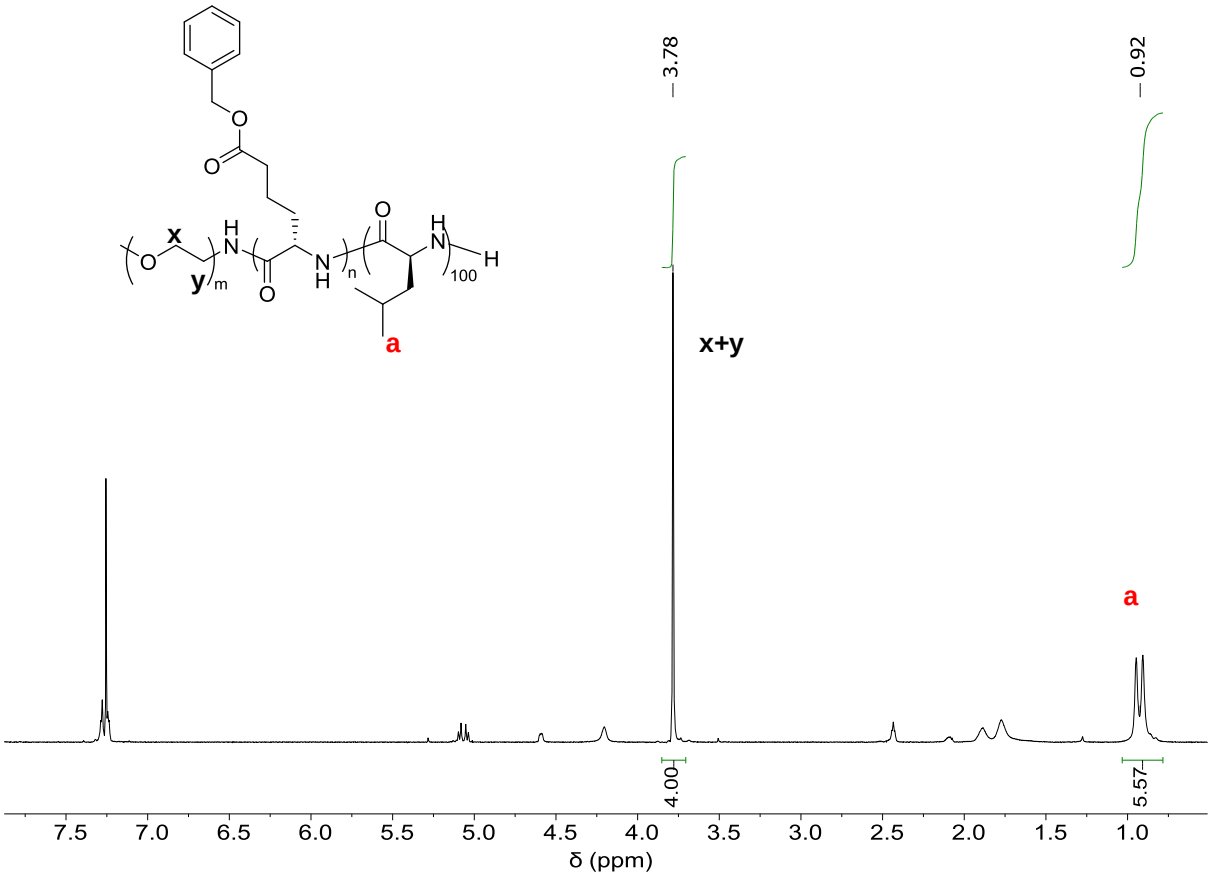

Figure S17. ^{1}H NMR spectrum (500 MHz) of PEG-polypeptides with PLeu$_{100}$ in $CDCl_3$/TFA-*d* (85:15, v/v) prepared from streamlined synthesis.

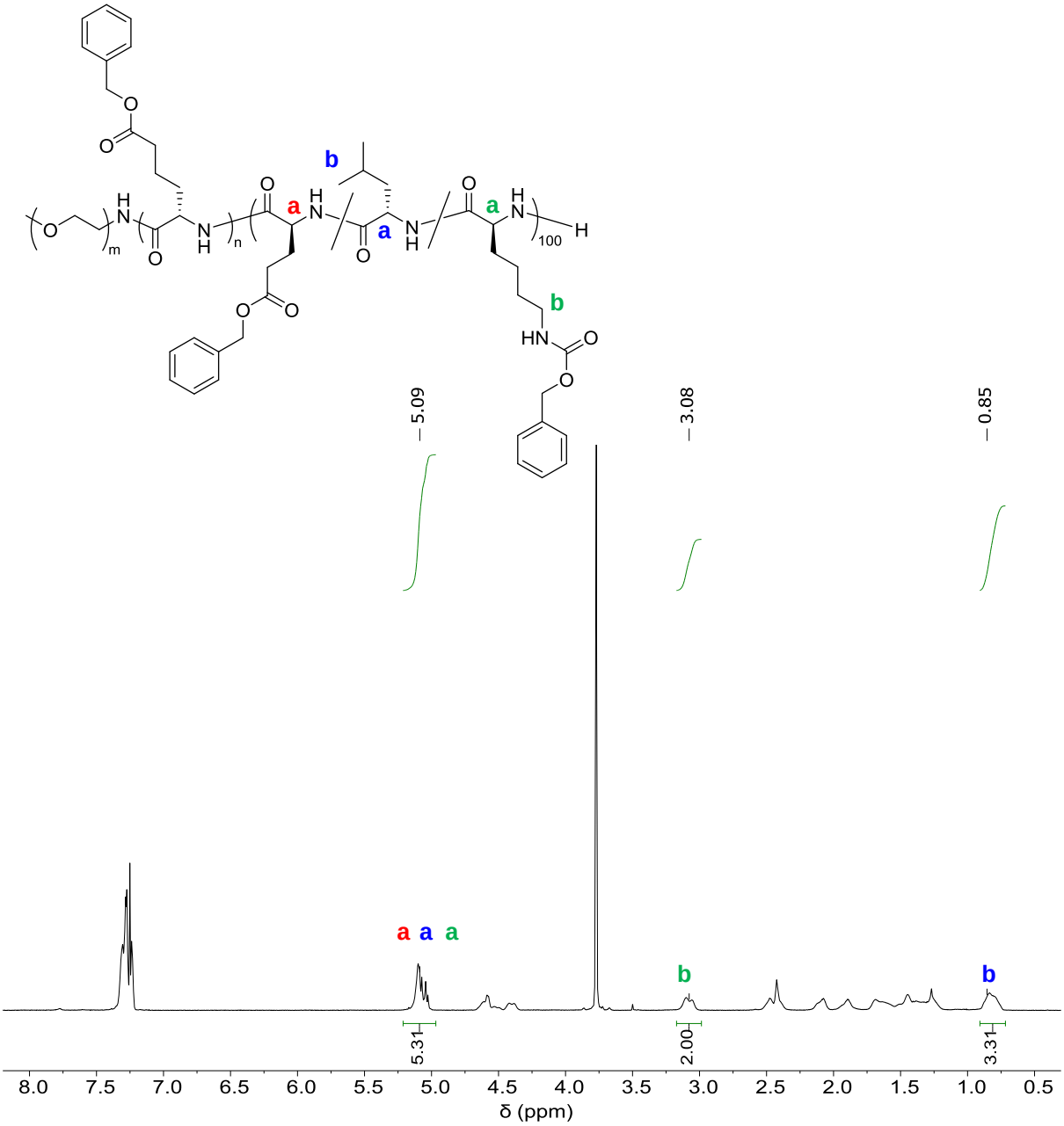

Figure S18. ^{1}H NMR spectrum (750 MHz) of PEG-polypeptide with PBLG$_{40}$-*r*-PZLL$_{40}$-*r*-PLeu$_{20}$ (designed 2:2:1) in $CDCl_3$/TFA-*d* (85:15, v/v) prepared from streamlined synthesis.

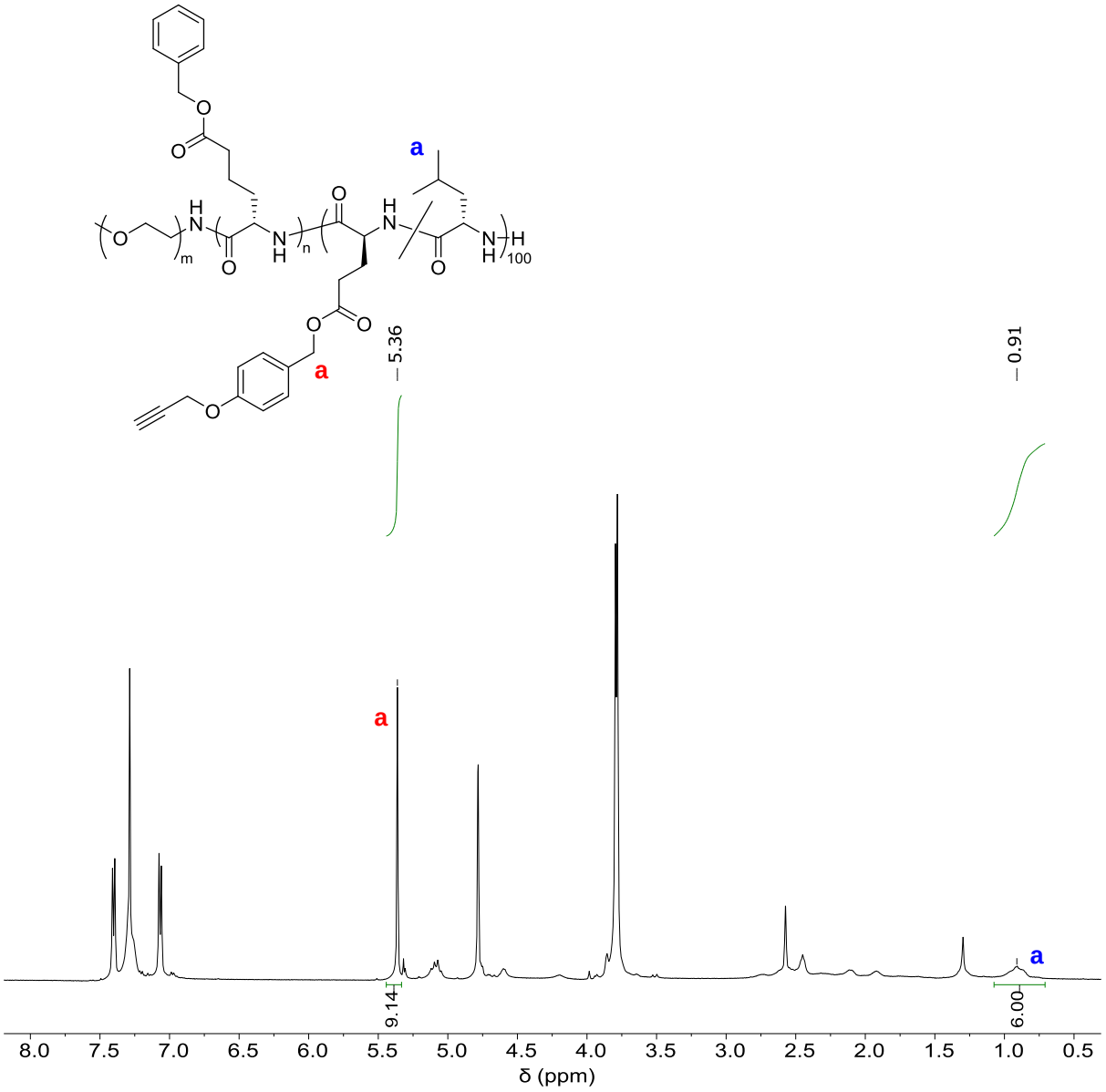

Figure S19. ^{1}H NMR spectrum (750 MHz) of PEG-polypeptide with PPOB$_{80}$-*r*-PLeu$_{20}$ (designed 4:1) in $CDCl_3$/TFA-*d* (85:15, v/v) prepared from streamlined synthesis.

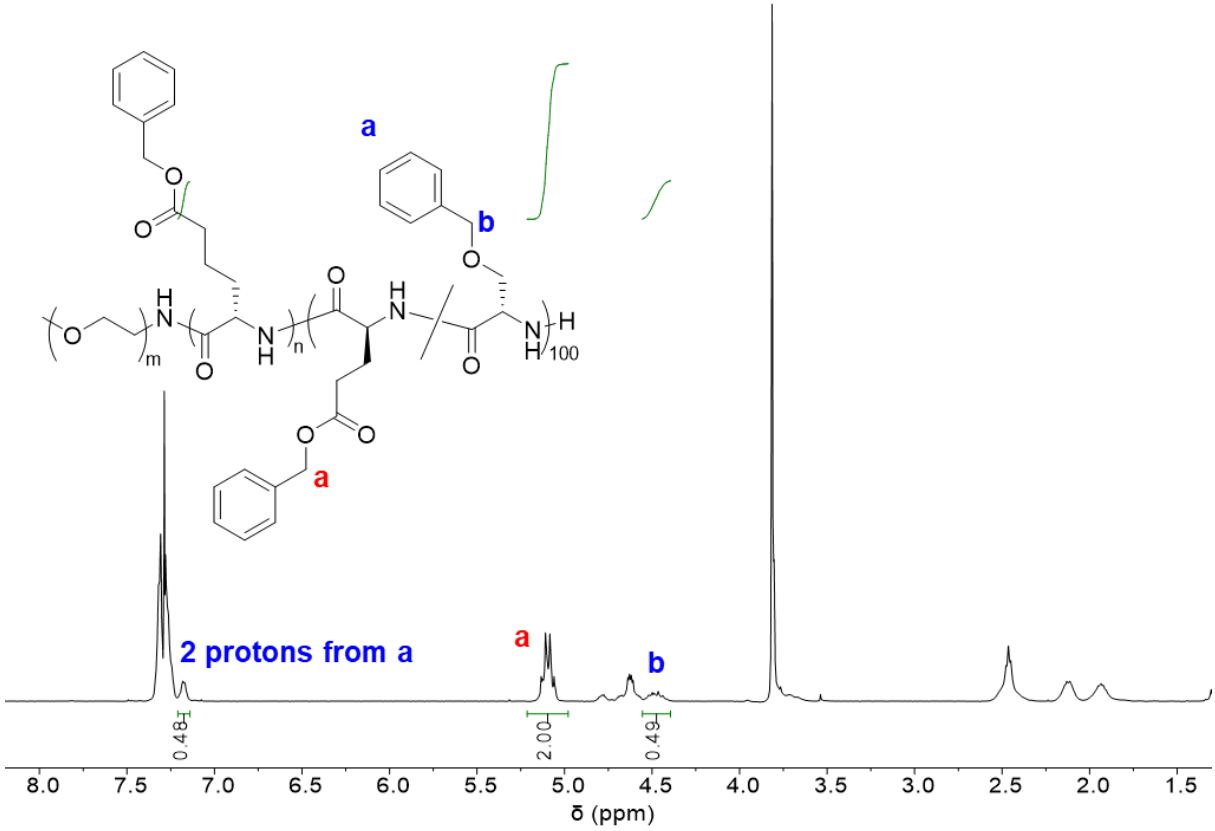

Figure S20. ^{1}H NMR spectrum (750 MHz) of PEG-polypeptide with PBLG$_{75}$-*r*-PBLS$_{25}$ (designed 3:1) in $CDCl_3$/TFA-*d* (85:15, v/v) prepared from streamlined synthesis.

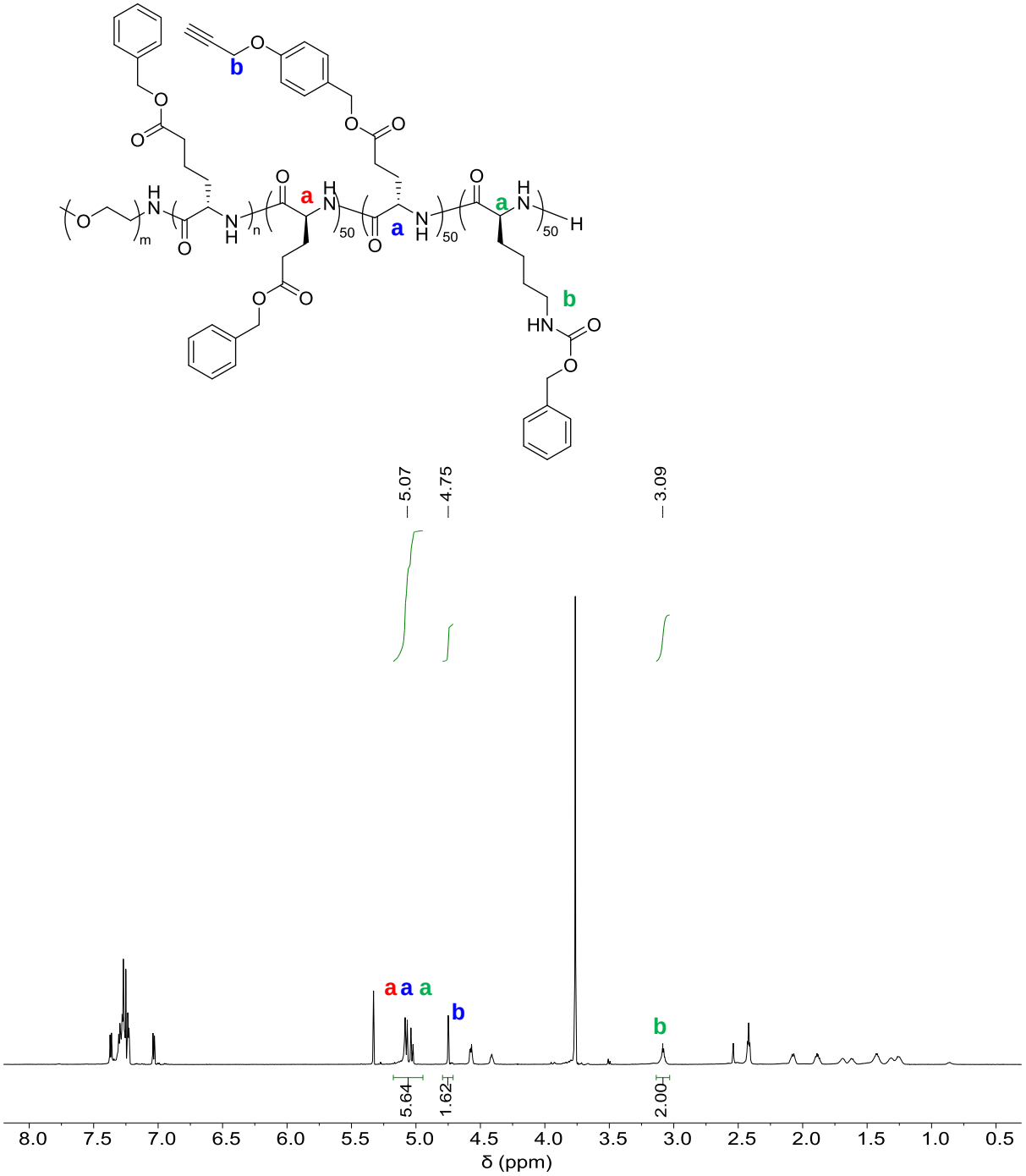

Figure S21. ^{1}H NMR spectrum (750 MHz) of PEG-polypeptide with PBLG$_{50}$-*b*-PPOB$_{50}$-*b*-PZLL$_{50}$ in $CDCl_3$/TFA-*d* (85:15, v/v).

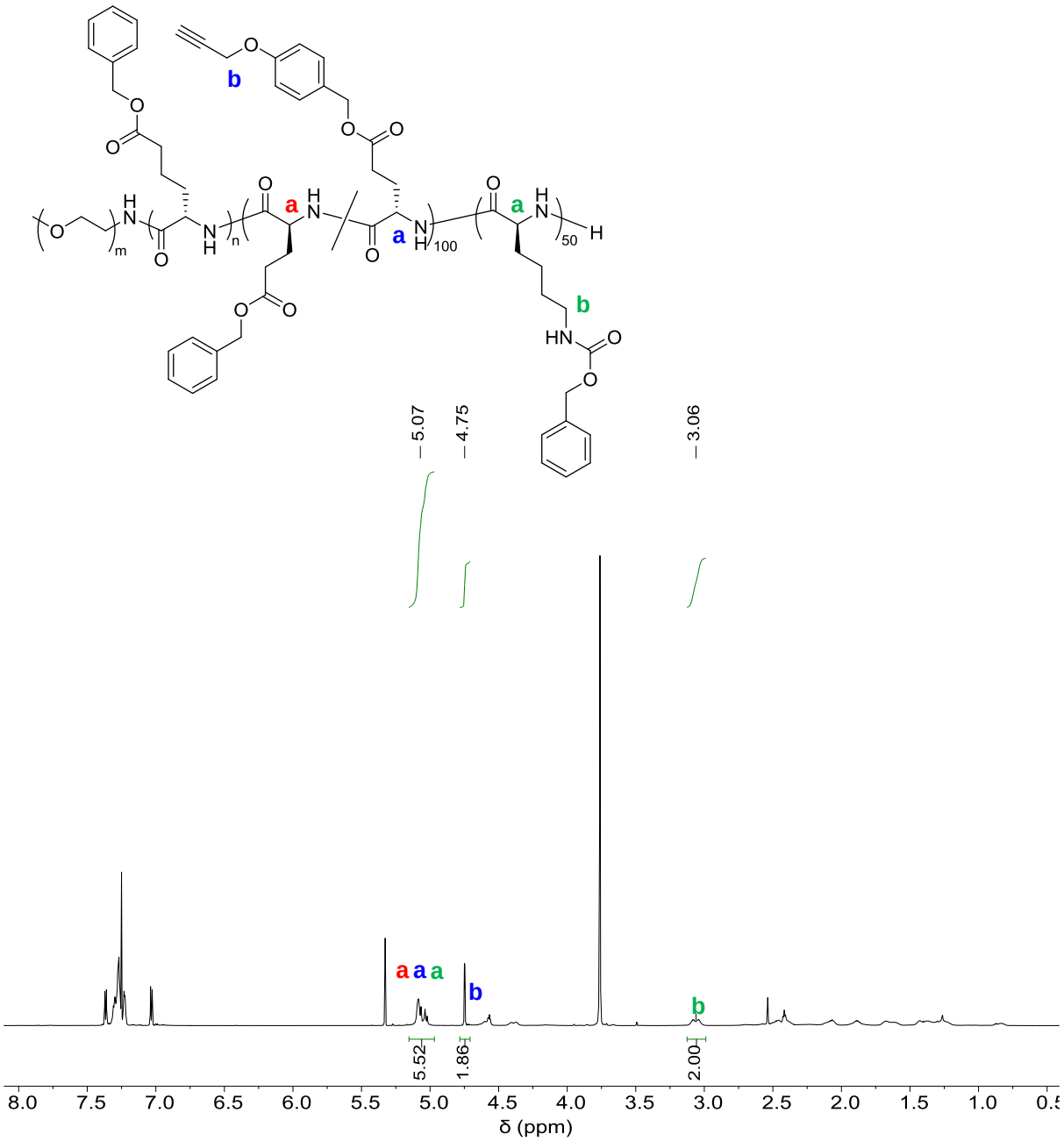

Figure S22. ^{1}H NMR spectrum (750 MHz) of PEG-polypeptide with (PBLG$_{50}$-*r*-PPOB$_{50}$)-*b*-PZLL$_{50}$ in $CDCl_3$/TFA-*d* (85:15, v/v).

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