

Supporting information
for

A simple glovebox-free strategy to significantly accelerate the syntheses of well-defined polypeptides by *N*-carboxyanhydride (NCA) ring opening polymerizations

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Experimental section:

Materials. *N,N*-dimethylformamide (DMF), diethyl ether, dichloromethane (DCM), tetrahydrofuran (THF), hexane, ethylacetate, γ -benzyl-L-glutamate, *n*-hexylamine and triphosgene were purchased from Sigma-Aldrich company (USA). All other chemicals were used without further purification, unless otherwise noted.

Instrumentation.

^1H and ^{13}C NMR spectra were recorded on Varian Inova 300 MHz or Varian Mercury 300 MHz spectrometers interfaced to a UNIX computer using VnmrJ software. Chemical shifts were referenced to solvent resonance signals. IR spectra were recorded on an IR Prestige 21 system (Shimadzu Corp., Japan) and analyzed using IRsolution v. 1.40 software.

N,N-dimethylformamide-based gel permeation chromatography (DMF GPC) was conducted on a Waters Chromatography, Inc. (Milford, MA) system equipped with an isocratic pump model 1515, a differential refractometer model 2414 and a two-column set of Styragel HR 4 and HR 4E 5 mm DMF 7.8 x 300 mm columns. The system was equilibrated at 70 °C in pre-filtered DMF containing 0.05 M LiBr, which served as polymer solvent and eluent (flow rate set to 1.00 mL/min). Polymer solutions were prepared at concentrations of *ca.* 3 mg/mL and an injection volume of 0.2 mL was used. Data collection and analysis was performed with Empower Pro software. The system was calibrated with poly(ethylene glycol) standards (Polymer Laboratories, Amherst, MA) ranging from 615 to 442,800 Da.

Glass transition temperatures (T_g) were measured by differential scanning calorimetry on a Mettler-Toledo DSC822[®] (Mettler-Toledo, Inc., Columbus, OH), with a heating rate of 10 °C /min. Measurements were analyzed using Mettler-Toledo STAR[®] v. 7.01 software. The T_g was taken as the midpoint of the inflection tangent, upon the third heating scan. Thermogravimetric analysis was performed under Argon atmosphere using a Mettler-Toledo model TGA/SDTA851[°], with a heating rate of 5 °C /min. Measurements were analyzed by using Mettler-Toledo STAR[®] v. 7.01 software.

The control experiments were conducted in the glove box of SG1200/750TS model, produced by Vigor Gas Purification Technologies Inc. Box pressure was stabilized at 2.70 mbar Argon (>99%). Oxygen and moisture were lower than 3 ppm. Temperature was stabilized

between 28.3 °C and 28.6 °C.

Synthesis of BLG-NCA¹

The BLG-NCA was synthesized according to the literature method.¹

General procedure for the polymerization of BLG-NCA

In a 10 mL flame dried Schlenk flask equipped with a magnetic stir bar, BLG-NCA (250 mg, 0.96 mmol) was dissolved in dry DMF (5.0 mL). *n*-Hexylamine (0.48 mg, 0.0048 mmol) in a stock solution (40 μ L, 0.12 mmol/mL) was added directly into the monomer solution and was stirred under continuous N₂ flow (250 mL/min). The Schlenk flask was capped with a rubber stopper with a needle outlet connected to a tube filled with drying agent. The reaction mixture was stirred at room temperature with a stir rate of 340 rpm, and aliquots were collected by syringe for determination of NCA concentration by measuring the intensity of the NCA anhydride peak at 1788 cm⁻¹ using ATR-FTIR. The conversion of NCA monomer was determined by comparing the NCA concentration in the reaction with the initial NCA concentration. All the kinetics studies were conducted at least twice and standard derivations were less than 0.05. The detailed characterization of one typical polymer PBLG₄₇ was conducted. ¹H NMR (300 MHz, TFA-D, ppm): δ 0.79 (s, CH₃CH₂CH₂), 1.75-2.25 (br, CHCH₂CH₂), 2.28-2.70 (s, br, CH₂CH₂CO), 4.50-4.80 (br, COCHNH), 4.90-5.20 (br, COOCH₂), 7.11-7.27 (br, ArH). ¹³C NMR (300 MHz, TFA-D, ppm): δ 26.6, 29.8, 53.2, 68.4, 127.9, 128.3, 128.5, 134.1, 173.3, 175.8. FT-IR (cm⁻¹): 3292, 3034, 2953, 1728, 1649, 1545, 1452, 1389, 1252, 1121, 966, 741, 694. (*T*_g) = 19.5 °C. TGA in Argon: 25-280 °C: 0% mass loss, 280-360 °C: 70 % mass loss, 360-500 °C: 8 % mass loss, 22 % mass remaining above 500 °C.

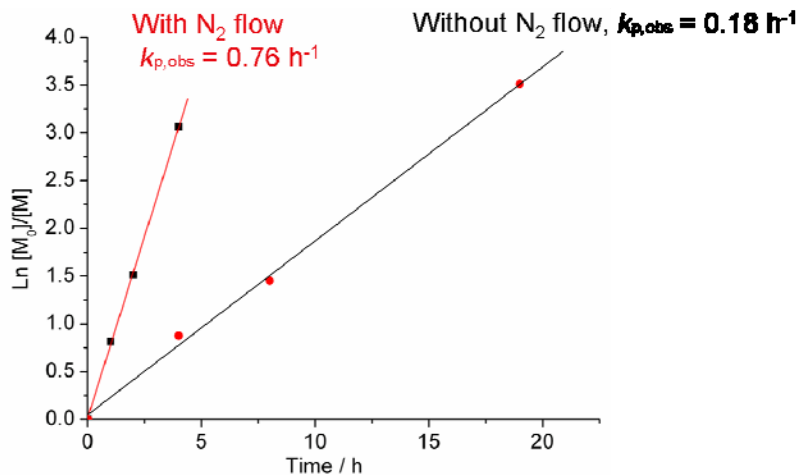


Figure S1. The kinetic study of *n*-hexylamine initiated BLG-NCA polymerization at a BLG-NCA : I ratio of 50 : 1 at room temperature (The NCA ROP without N₂ flow was conducted in the glove box). The initial BLG-NCA concentration was 50 mg/mL.

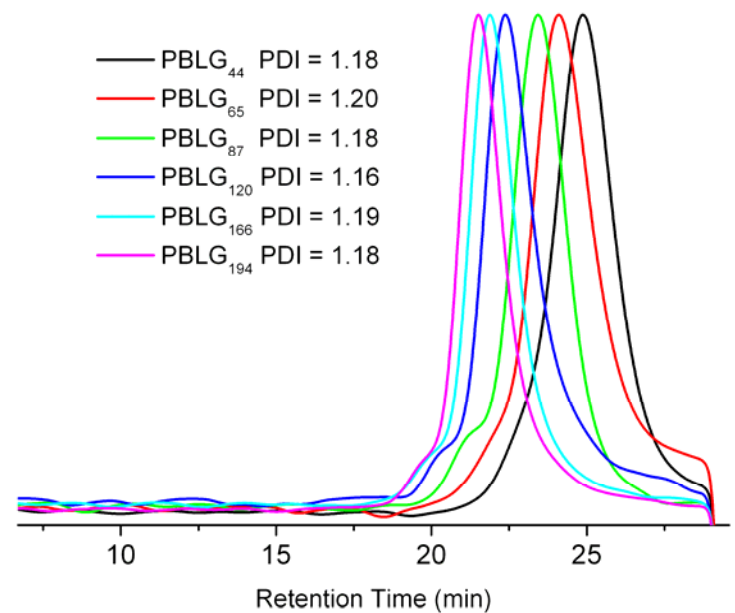


Figure S2. The GPC traces of N₂ flow accelerated NCA-ROP of PBLG quenched at determined time with different degree of polymerization.

Reference:

1. D. S. Poche, M. J. Moore and J. L. Bowles, *Synthetic Commun*, **1999**, *29*, 843-854.