Supporting information for manuscript entitled with

Organobase 1,1,3,3-Tetramethyl Guanidine Catalyzed Rapid Ring-opening Polymerization of α-Amino Acid N-carboxyanhydrides Adaptive to Amine, Alcohol and Carboxyl Acid Initiators

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Materials

Moisture-sensitive compounds were handled in an glovebox . Tetrahydrofuran (Alfa Aesar) was dried by refluxing over sodium and distilling under a nitrogen atmosphere. Benzyl alcohol (Alfa Aesar) was distilled from CaH_2. Benzylamine (Alfa Aesar) was refluxed with NaOH for 24 hours and then distilled under reduced pressure. Benzoic acid (Macklin) was dried in vacuum. 1,1,3,3-Tetramethylguanidine (innochem) was used as received without further purification unless otherwise noted.

Preparation of γ-benzyl-$_L$-glutamate *N*-carboxyanhydride NCA (BLG NCA)

To a mixture of γ-benzyl-$_L$-glutamic acid (5 g, 0.021mol) and triphosgene (4.5 g ,0.015 mol) under nitrogen was added anhydrous THF (200 mL). The solution was then heated to 50 °C for 4h, after which the solvent was removed under vacuum. A clear and colorless solution was obtained. The solvent was removed under vacuum. The residue (crude NCA) was transferred to a glovebox, dissolved in ca. 25 mL dry THF and recrystallized by layering 3 volumes of dry hexanes, and allowing to stand for 48 h. This procedure was repeated three times to yield a white crystalline (40%).

Preparation of N^ε-benzyloxycarbonyl-$_L$-lysine-*N*-carboxyanhydride NCA (ZLL NCA)

To a mixture of N^ε-benzyloxycarbonyl-$_L$-lysine (5 g, 0.016mol) and triphosgene (3.3 g ,0.011 mol) under nitrogen was added anhydrous THF (200 mL). The solution was then heated to 50 °C for 4h, after which the solvent was removed under vacuum. A clear and colorless solution was obtained. The

solvent was removed under vacuum. The residue (crude NCA) was transferred to a glovebox, dissolved in ca. 25 mL dry THF and recrystallized by layering 3 volumes of dry hexanes, and allowing to stand for 48 h. This procedure was repeated three times to yield a white crystalline (60%).

Typical polymerization of BLG-NCA

BLG-NCA was placed in a vial and dissolved in THF. Benzoic acid/benzyl amine/benzyl alcohol ($PhCOOH/BzNH_2/BzOH$, 0.1 M in THF) and TMG (0.1 M in THF) was added at the proper $[M]_0/[I]_0$ ratios ensuring the final concentration of $[M]_0 = 0.10$ M. The reaction was stirred at room temperature. After the polymerization was complete, the obtained polymer was dissolved in GPC mobile phase for GPC analysis.

Methods

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AVNEO400ASCEND FT-NMR spectrometer at 400 MHz for ^1H NMR. Matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF MS) analyses were conducted on a Bruker Microflex LRF MS spectrometer equipped with a 337 nm nitrogen laser operating in a positive ion, linear mode. The sample solutions (20 mg/mL in THF), trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene] malononitrile (DCTB) solution (40 mg/mL in THF) and sodium trifluoroacetate aqueous solution (5 mg/mL) were mixed in a volume ratio of 4:4:2, 1μL of which was then deposited on the target plate and dried before measurement. Size exclusion chromatography (SEC) experiments were performed on an Agilent HPLC system equipped with a model 1260 Hip degasser, a model 1260 Iso pump and a model 1260 differential refractometer detector. The system was equilibrated at 40 °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). The sample concentration used for SEC analyses was 5 mg/mL. Data collection and analysis was performed with Empower Pro software. The system was calibrated with polystyrene standards ranging from 600 to 904,700 Da. Fourier transform infrared (FTIR) spectra were performed using a Jasco FT/IR-4700 spectrometer in a SL-3 Model 0.1 mm KBr permanent sealed liquid cell (International Crystal Laboratories).

Table S1. Polymerization of BLG NCA in THF.

entry	monomer	initiator	$[M]_0$:$[I]_0$:[TMG]	M_n[a] (kDa)	M_n[b] (kDa)	M_w/M_n
1	BLG NCA	N/A	100:0:1	21.9	73.0	1.30
2	BLG NCA	PhCOOH	20:1:1	4.4	18.0	1.43
3	BLG NCA	$BzNH_2$	20:1:1	4.4	7.1	1.46
4	BLG NCA	BzOH	20:1:1	4.4	9.2	1.55
5	BLG NCA	PhCOOH	50:1:1	10.9	56.2	1.25
6	BLG NCA	$BzNH_2$	50:1:1	10.9	29.6	1.35
7	BLG NCA	BzOH	50:1:1	10.9	39.7	1.36
8	BLG NCA	PhCOOH	100:1:1	21.9	105.0	1.28
9	BLG NCA	$BzNH_2$	100:1:1	21.9	45.7	1.19
10	BLG NCA	BzOH	100:1:1	21.9	60.2	1.19
11	BLG NCA	PhCOOH	150:1:1	32.8	185.4	1.33
12	BLG NCA	$BzNH_2$	150:1:1	32.8	144.4	1.22
13	BLG NCA	BzOH	150:1:1	32.8	102.9	1.32
14	ZLL NCA	PhCOOH	50:1:1	13.1	41.4	1.34
15	ZLL NCA	$BzNH_2$	50:1:1	13.1	12.5	1.34
16	ZLL NCA	BzOH	50:1:1	13.1	13.0	1.37
17	BLG NCA+ZLL NCA	PhCOOH	(20+20):1:1	9.6	42.2	1.37
18	BLG NCA+ZLL NCA	$BzNH_2$	(20+20):1:1	9.6	22.5	1.30
19	BLG NCA+ZLL NCA	BzOH	(20+20):1:1	9.6	26.7	1.31
20	BLG NCA	PEG_{1000}-COOH	100:1:1	22.9	80.5	1.54
21	BLG NCA	PEG_{750}-OH	100:1:1	22.6	50.0	1.40

[a] Expected molecular weight; [b] determined via gel permeation chromatography.

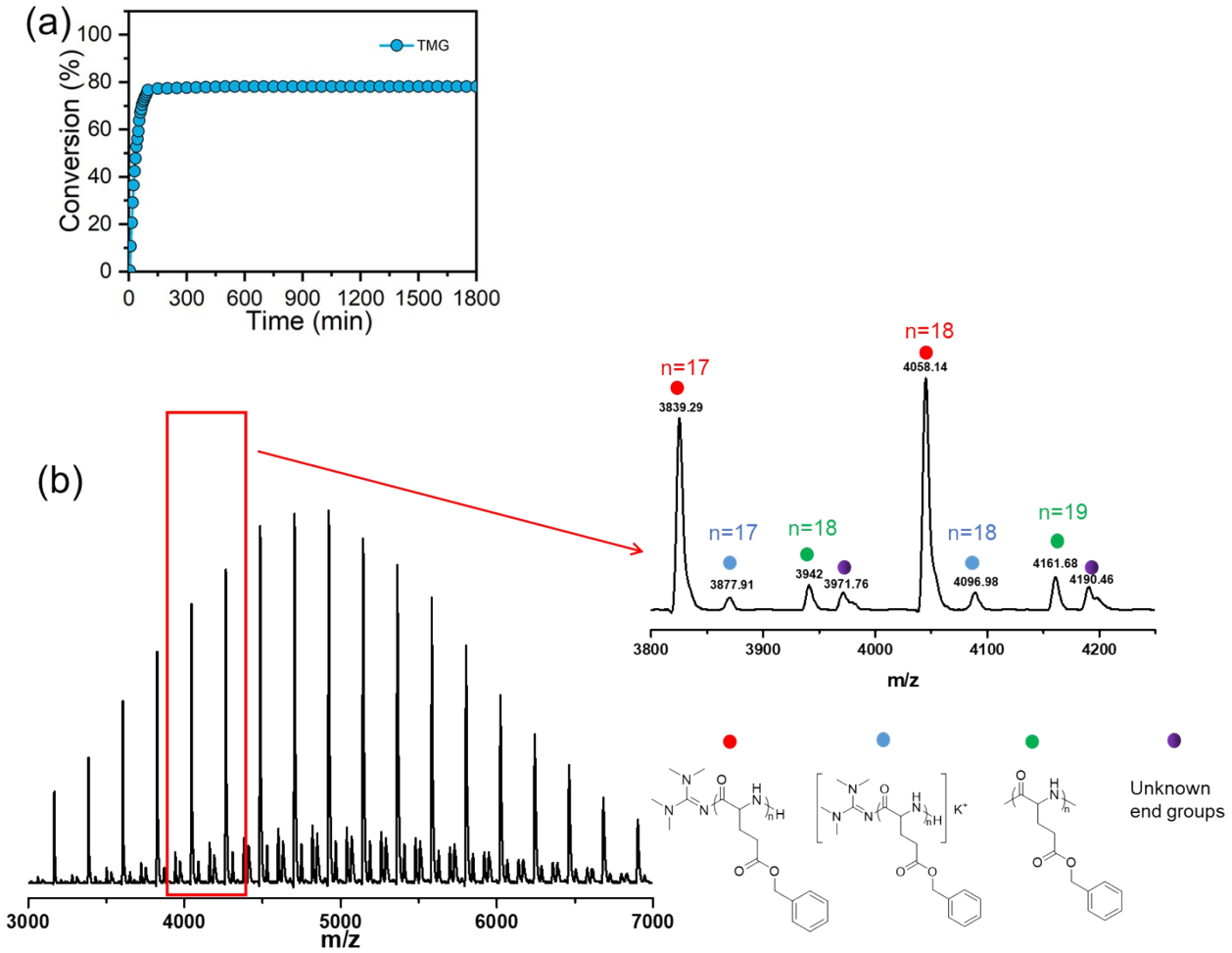

Fig. S1 The polymerization of BLG NCA initiated by TMG in THF: (a) Conversion of NCA as measured by FTIR spectrum over the duration of the polymerization ($[M]_0/[I]_0$=100:1). (b) MALDI-TOF MS spectra of PBLG under the standard conditions ($[M]_0$ =0.1 M, $[M]_0$:$[I]_0$ = 20:1, THF, 25 °C). In addition, the green species may be corresponding to the cyclic polypeptides.[1, 2]

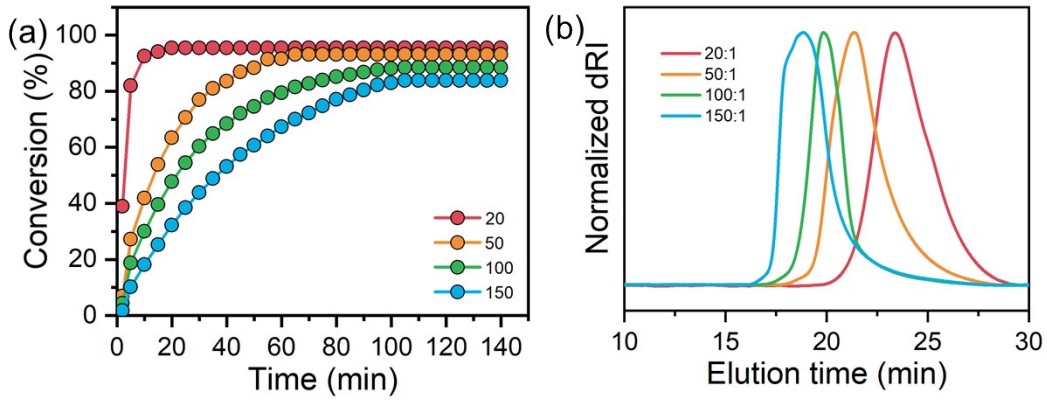

Fig. S2 The polymerization of BLG NCA initiated by benzoic acid/TMG in THF ($[M]_0/[I]_0$=20:1, 50:1, 100:1, 150:1, $[M]_0$ = 0.1 M, $[I]_0$/[TMG]=1:1): (a) Conversion of NCA as measured by FTIR spectrum over the duration of the polymerization and (b) overlay of the GPC curves.

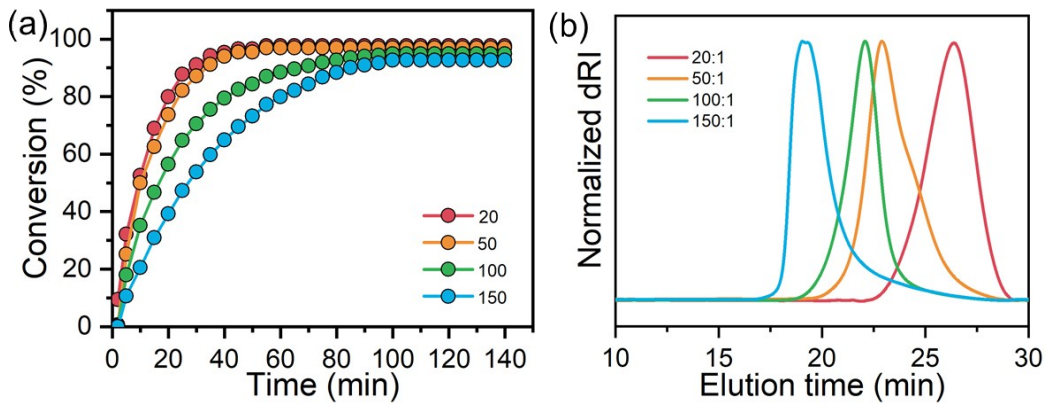

Fig. S3 The polymerization of BLG NCA initiated by benzyl amine/TMG in THF ($[M]_0/[I]_0$=20:1, 50:1, 100:1, 150:1, $[M]_0$ = 0.1 M, $[I]_0$/[TMG]=1:1): (a) Conversion of NCA as measured by FTIR spectrum over the duration of the polymerization and (b) overlay of the GPC curves.

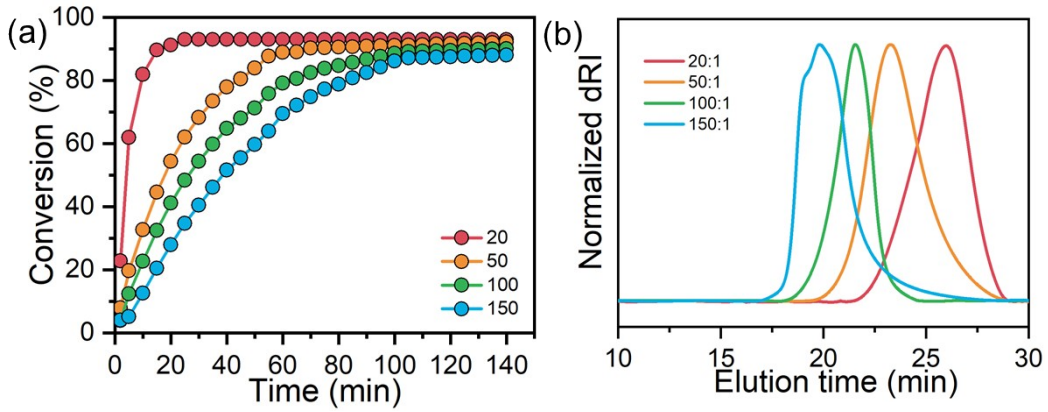

Fig. S4 The polymerization of BLG NCA initiated by benzyl alcohol/TMG in THF ($[M]_0/[I]_0$=20:1, 50:1, 100:1, 150:1, $[M]_0$ = 0.1 M, $[I]_0$/[TMG]=1:1): (a) Conversion of NCA as measured by FTIR spectrum over the duration of the polymerization and (b) overlay of the GPC curves.

References

1. L. Guo and D. Zhang, *J. Am. Chem. Soc.*, 2009, **131**, 18072-18074.
2. A. Li, L. Lu, X. Li, L. He, C. Do, J. C. Garno and D. Zhang, *Macromolecules*, 2016, **49**, 1163-1171.