# Supporting Information for Manuscript Entitled with Ultrafast ring-opening copolymerization of lactide with glycolide toward random poly(lactic-*co*-glycolic acid) copolymers by organophosphazene base and urea binary catalysts

Yong Shen, \*,<sup>a</sup> Dong Li,<sup>a</sup> Xinhui Kou,<sup>b</sup> Rui Wang,<sup>a</sup> Fusheng Liu<sup>\*,a</sup> and Zhibo Li<sup>\*,a, c</sup>

<sup>a</sup> State Key Laboratory Base of Eco-Chemical Engineering; College of Chemical

Engineering, Qingdao University of Science and Technology, Qingdao 266042,

China.

<sup>b</sup> Analyses and testing center, Qingdao University of Science and Technology,

Qingdao 266042, China.

<sup>c</sup> Key Laboratory of Biobased Polymer Materials, Shandong Provincial Education

Department; Qingdao University of Science and Technology, Qingdao 266042,

China.

Corresponding Author: E-mail: <a href="mailto:shenyong@qust.edu.cn">shenyong@qust.edu.cn</a>

E-mail: liufusheng63@sina.com

E-mail: zbli@qust.edu.cn

## **Experimental section**

### Materials.

Tetrahydrofuran (THF) and toluene (TOL) were purified by purging with dry nitrogen, followed by passing through columns of activated alumina. N, N-dimethylformamide (DMF) was refluxed with CaH<sub>2</sub> for 4 hours and then distilled

1

under reduced pressure. Potassium methoxide (KOMe) and 1-*tert*-butyl-2, 2, 4, 4, 4pentakis(dimethylamino)- $2\lambda^5$ ,  $4\lambda^5$ -catenadi-(phosphazene) (*t*-BuP<sub>2</sub>) were purchased from Sigma-Aldrich Chemical Co. Benzyl alcohol (BnOH) purchased from Aladdin reagent Co. was stirred with CaH<sub>2</sub> for 24 hours, distilled under reduced pressure and then stored in a glovebox. L-Lactide (L-LA) and glycolide (GA) purchased from Medichem reagent Co. were purified by recrystallization three times from dry-toluene, then stored at -20 °C in a glovebox before use. The cyclic trimeric phosphazene base (CTPB) was synthesized according to the reported procedure.<sup>1</sup> The ureas used in this study were prepared according to the previous report.<sup>2</sup> All commercially obtained reagents were used as received without further purification unless otherwise noted.

#### Instruments.

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AVNEO400ASCEND FT-NMR spectrometer at 400 MHz for <sup>1</sup>H NMR and 100 MHz for <sup>13</sup>C NMR. Chemical shifts were reported in  $\delta$  (ppm) with the residual deuterated solvent peak as reference. Monomer conversions and the copolymer compositions were determined by <sup>1</sup>H-NMR spectroscopy measured in CDCl<sub>3</sub>. The LA conversion was calculated according to the formula Conv.(LA, %) =  $I_{5.19\ ppm}/(I_{5.19\ ppm}+\ I_{5.04}$ ppm)×100%. The GA conversion was calculated according to the formula Conv.(GA, %) =  $I_{4.77}$  ppm/( $I_{4.77 \text{ ppm}} + I_{4.94 \text{ ppm}}$ )×100%. GA incorporation into the copolymers was calculated according to the formula  $F_{\rm GA}$  (%) =  $I_{4.77 \text{ ppm}}/(2I_{5.19 \text{ ppm}} + I_{4.77})$ <sub>ppm</sub>)×100%. Quantitative <sup>13</sup>C NMR spectra were recorded to determine the relative fractions of dyad repeating unit sequences. The quantitative <sup>13</sup>C NMR spectra (100 MHz) were recorded with a pulse sequence of zgig. The scan time and the acquisition time was 5120 and 0.45 s, respectively. The pulse width was 10 µs, and delay between pulses was 5 s. 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 (10 *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene] mg/mL THF). in 2

malononitrile (DCTB) solution (50 mg/mL in THF) and sodium trifluoroacetate aqueous solution (5 mg/mL) were mixed in a volume ratio of 4:2:1, 1 µL of which was then deposited on the target plate and dried before measurement. Size exclusion chromatography (SEC) experiments were performed on a Agilent HPLC system equipped with a model 1260 Hip degasser, a model 1260 Iso pump and a model 1260 differential refractometer detector with using THF as mobile phase at a flow rate of 1.0 mL/min at 40 °C. One PLgel 5 µm guard column and three Mz-Gel SD<sub>plus</sub> columns (10<sup>3</sup> Å, 10<sup>4</sup> Å, and 10<sup>5</sup> Å, linear range of MW = 1000 - 2\*10<sup>6</sup> Da) were connected in series. The molecular weights and dispersities were calculated using 10 polystyrene standards with narrow molecular weight distribution as references. The sample concentration used for SEC analyses was 5-10 mg/mL. Differential scanning calorimetry (DSC) measurements were performed on a TA instrument DSC 25. Temperature was calibrated with an indium standard. Measurements were performed under N<sub>2</sub> atmosphere with a flow rate of 50 mL/min. Each sample with a mass of 5-10 mg was used for the measurement. The typical procedures were described as follows: in the first heating scan, samples were heated from -50 °C to 230 °C at a heating rate of 10 °C/min and kept at 230 °C for 2 min to eliminate any thermal history. In the second heating scan, samples were cooled to -50 °C at 10 °C/min and then equilibrium at -50 °C for 2 min, and subsequently reheated to 230 °C at 10 °C/min. Thermogravimetric analysis (TGA) measurements were performed on a STA 8000 thermogravimetric analyzer. The samples were heated from 40 °C to 600 °C at a heating rate of 20 °C/min under N<sub>2</sub> atmosphere with a flow rate of 40 mL/min.

Run	M/B/U/I	T (°C)	[M] (mol/L)	Conv. <sup>b</sup> (LA%)	Conv. <sup>b</sup> (GA%)	F <sub>GA</sub> <sup>b</sup>	$M_{ m n}$ , theo <sup>c</sup>	M <sub>n</sub> , sec <sup>d</sup> (kDa)	$D^{\mathrm{d}}$
			( )		( )		(kDa)		
1	100/1/3/1	0	1	98	>99	29	13.4	10.4	1.83
2	100/1/3/1	-20	1	96	>99	30	13.2	12.6	1.92
3	100/1/3/1	RT	0.5	93	>99	30	12.9	9.6	2.00

Table S1. Results of ROCOP of LA with GA catalyzed by a base/urea binary catalyst <sup>a</sup>

4	100/1/3/1	RT	0.1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
---	-----------	----	-----	------	------	------	------	------	------

<sup>a</sup> Conditions: 0.05 mmol benzyl alcohol (BnOH) was used as the initiator. The copolymerizations were conducted at [LA]/[GA]/[CTPB]/[U2]/[BnOH] = 70/30/1/3/1 in THF within 1 minute. n.d.= not determined due to the precipitation of resultant copolymer. <sup>b</sup> Monomer conversions, and molar percentage of GA in the copolymers ( $F_{GA}$ ) were determined by <sup>1</sup>H-NMR spectroscopy. <sup>c</sup> Theoretical molecular weight calculated from the feeding molar ratio and monomer conversion as  $M_{n, theo} = [LA]/[I] * \text{conv.}(LA) * MW(LA) + [GA]/[I] * \text{conv.}(GA) * MW(GA) +$ MW(Initiator). <sup>d</sup> Determined by SEC in THF at 40 °C relative to PS standards.

Run		LA/GA	Conv. <sup>b</sup>	Conv. <sup>b</sup>	E = h(0/)	M <sub>n, theo</sub> c (kDa)	M <sub>n, SEC</sub> <sup>d</sup> (kDa)	Dd
	M/B/U/I		(LA%)	(GA%)	$F_{\rm GA}$ ° (%)			D
1	35/1/3/1	7/3	97	>99	30	4.7	4.6	1.71
2	50/1/3/1	7/3	97	>99	31	6.7	6.0	1.84
3	75/1/3/1	7/3	97	>99	30	10.0	8.2	1.83
4	100/1/3/1	7/3	97	>99	30	13.3	11.5	1.86
5	120/1/3/1	7/3	97	>99	30	16.0	13.0	2.04

Table S2. The molecular weights and distributions of PLGA copolymers obtained at different feeding molar ratio <sup>a</sup>

<sup>a</sup> Conditions: 0.05 mmol benzyl alcohol (BnOH) was used as initiator, CTPB and U2 was used as base and urea, respectively. The copolymerizations were conducted at ambient temperature with a total monomer concentration of 1M in THF within 1 minute. <sup>b</sup> Monomer conversions and molar percentage of GA in the copolymers ( $F_{GA}$ ) were determined by <sup>1</sup>H-NMR spectroscopy. <sup>c</sup> Theoretical molecular weight calculated from the feeding molar ratio and monomer conversion as  $M_{n, \text{ theo}} = [LA]/[I] * \text{ conv.}(LA) * MW(LA) + [GA]/[I] * \text{ conv.}(GA) * MW(GA) + MW(Initiator). <sup>d</sup> Determined by SEC in THF at 40 °C relative to PS standards.$ 

Table	S3.	The	copolymerization	results	of	LA	with	GA	for	reactivity	ratios
determ	inati	on <sup>a</sup>									

Run	$[LA]_0$	$[GA]_0$	Conv. <sup>b</sup>	Conv. <sup>b</sup>	[LA] <sup>c</sup>	[GA] <sup>c</sup>
		L ]\$	(LA, %)	(GA, %)		
1	0.91	0.09	53	75	0.43	0.02
2	0.86	0.14	26	37	0.64	0.09
3	0.72	0.28	30	35	0.51	0.18
4	0.52	0.48	21	19	0.41	0.39
5	0.33	0.67	19	13	0.27	0.58

<sup>a</sup> Conditions: (2.5  $\mu$ mol, 3 mg) CTPB was used as base. [LA + GA]<sub>0</sub>/[CTPB]/[U2]/[BnOH] = 100/0.05/0.15/10. The copolymerizations were conducted at ambient temperature with a total monomer concentration of 1M in THF within 3 s. <sup>b</sup> Monomer conversions were measured by <sup>1</sup>H NMR spectra. <sup>c</sup> [LA] = [LA]<sub>0</sub> \* (1-Conv.(LA)), [GA] = [GA]<sub>0</sub> \* (1-Conv.(GA)).

Entry	Sample	$F_{\rm GA}$	M <sub>n</sub>	Đ	T <sub>d, 5%</sub>	T <sub>d, max</sub>	T <sub>g, DSC</sub> <sup>b</sup>	T <sub>g, Cal.</sub> <sup>c</sup>	T <sub>m</sub> <sup>b</sup>
			(kDa)		(°C)	(°C)	(°C)	(°C)	(°C)
1	PLLA	0	6.9	1.23	324.0	345.7	48.6		136
2	PLGA-1	11	6.2	1.85	347.7	387.7	42.6	44.0	
3	PLGA-2	31	6.0	1.84	287.8	367.4	30.0	37.9	
4	PLGA-3	49	6.5	1.76	311.8	391.2	17.1	29.7	

Table S4. TGA and DSC results of PLLA homopolymer and PLGA copolymers with various GA incorporations <sup>a</sup>

<sup>a</sup> PLLA was prepared with a molar feeding ratio of [LA]/[CTPB]/[U2]/[BnOH] = 50/1/3/1 at R.T. for 1 min. PLGA-1 (Table 1, run 8); PLGA-2 (Table 1, run 9); PLGA-3 (Table 1, run 10). <sup>b</sup> T<sub>g, DSC</sub> and T<sub>m</sub> were obtained from the second heating scans of DSC curves. <sup>c</sup> T<sub>g, Cal.</sub> was calculated according to Fox equation:  $1/T_g=W_1/T_{g1}+W_2/T_{g2}$  using T<sub>g</sub> of 10 °C for PGA homopolymer with a  $M_n < 10$  kDa.



**Figure S1.** <sup>13</sup>C NMR spectrum of PLGA copolymer (Table 1, run 9) measured in CDCl<sub>3</sub>.



Figure S2. SEC curves of PLGA copolymers prepared with different ureas.



**Figure S3.** <sup>1</sup>H-NMR spectrum of PLGA copolymer measured in CDCl<sub>3</sub> prepared by using BDM as the initiator.



**Figure S4.** <sup>1</sup>H-NMR spectrum of PLGA copolymer measured in CDCl<sub>3</sub> prepared by using Ph<sub>2</sub>CHOH as the initiator.



**Figure S5.** <sup>1</sup>H-NMR spectrum of PLGA copolymer measured in CDCl<sub>3</sub> prepared by using mPEG as the initiator.



Figure S6. SEC curves of mPEG-*b*-PLGA diblock copolymer (Table 1, run 14) and mPEG.





$$r_{LA} = \frac{lg^{[[LA]_0}/[[LA]]) - \frac{1}{p} lg^{[[0]_{[m]}} \frac{1 - p([GA]/[[LA]])}{1 - p([GA]_0/[[LA]_0)}}}{lg^{[[0]_{[m]}}(\int [[GA]]) + lg^{[[0]_{[m]}} \frac{1 - p([GA]/[[LA]])}{1 - p([GA]_0/[[LA]_0)}}}, \text{ where }$$

Lewis equation

p =

 $\frac{1 - r_{GA}}{1 - r_{LA}}$  (data shown in Table S3). The reactivity ratios of LA and GA was determined to be  $r_{LA} = 0.56$  and  $r_{GA} = 0.36$ , respectively.



Figure S8. The deconvolution of the carbonyl region of <sup>13</sup>C NMR spectrum of the PLGA copolymer with a  $F_{GA} = 49$  (Table 1, run 10).



Figure S9. (a) TGA and (b) DTG curves of PLLA homopolymer and PLGA 9





**Figure S10**. DSC curves (black lines: first heating scans; red lines: cooling scans; blue lines: second heating scans) of (a) PLLA homopolymer with a  $M_n = 6.9$  kDa, (b)  $F_{GA} = 11$  (Table 1, run 8), (c)  $F_{GA} = 31$  (Table 1, run 9), (d)  $F_{GA} = 49$  (Table 1, run 10).



**Figure S11**. DSC curves (black lines: first heating scans; red lines: cooling scans; blue lines: second heating scans) of PLLA homopolymer with a  $M_n = 14.1$  kDa.



Scheme S1. A plausible mechanism for the ROCOP of LA with GA using CTPB/urea

binary catalyst.

#### References

(1) Zhao, N.; Ren, C.; Li, H.; Li, Y.; Liu, S.; Li, Z. Selective Ring-Opening Polymerization of Non-Strained  $\gamma$ -Butyrolactone Catalyzed by A Cyclic Trimeric Phosphazene Base. *Angew. Chem. Int. Ed.* **2017**, *56*, 12987-12990.

(2) Shen, Y.; Xiong, W.; Li, Y.; Zhao, Z.; Lu, H.; Li, Z. Chemoselective Polymerization of Fully

Biorenewable  $\alpha$ -Methylene- $\gamma$ -Butyrolactone Using Organophosphazene/Urea Binary Catalysts Toward Sustainable Polyesters. *CCS Chem.* **2020**, *2*, 620-630.