

Supporting Information

Orthogonal Polymerization of Aziridine with Cyclic Carbonate for Constructing Amphiphilic Block Copolymers

Xiao-Hui Guo, Ge-Ge Gu, Tian-Jun Yue, Wei-Min Ren*

State Key Laboratory of Fine Chemicals, Dalian University of Technology,
Dalian 116024, China

E-mail: tjyue189@dlut.edu.cn

Contents

1. General information.
2. Experimental section.
3. Outputs of the copolymerization of BMA and TMC mediated by various Lewis Acids in the absence or presence of Lewis base.
4. ^1H NMR spectra of BMA/TMC copolymer synthesized from the copolymerization mediated by ZnCl_2 .
5. ^{13}C NMR spectra of PBMA, (*rac*)-BMA/TMC copolymer, and (*S*)-BMA/TMC copolymers.
6. HSQC spectra of (*S*)-BMA/TMC copolymer.
7. In-situ IR results of BMA/TMC copolymer synthesized from the copolymerization mediated by $\text{ZnCl}_2/\text{MTBD}$.
8. ^1H DOSY NMR spectra of of BMA/TMC copolymer synthesized from the copolymerization mediated by ZnCl_2 .
9. DSC curves of copolymers.
10. TGA curves of copolymers.
11. ^1H NMR spectra of PBMA-*b*-PTMC block copolymers with different PBMA contents.
12. Reference.

1. General information.

All the synthesis of compounds, involving air and/or water-sensitive were carried out in glove box or with the standard Schlenk techniques under dry nitrogen. 1,3-dioxan-2-one (TMC) was purchased from Adamas, was first dissolved in Tetrahydrofuran (THF) under nitrogen and stirred over CaH₂ for 2 days before being filtered and heated under vacuum for Solvents removal. 1-benzyl-2-methylaziridine (BMA) was distilled from CaH₂ under nitrogen for twice. ZnCl₂ (1 M in Tetrahydrofuran) that was supplied by Macklin reagent and 7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD) that was procured from Energy Chemical, were all used as received. ZnBr₂ and Zn(OAc)₂ were purchased from Energy Chemical and heated under vacuum for water removal.

Nuclear magnetic resonance (NMR). ¹H NMR spectra were recorded on a Varian INOVA-400 MHz type spectrometer and CDCl₃ were used as the solvent. The peak frequencies were referenced versus an internal standard TMS shift at 0.00 ppm for ¹H NMR.

Gel permeation chromatography (GPC). Molecular weights and molecular weight distributions of block polymers were measured by GPC analysis at 35 °C and a flow rate of 1.0 mL/min, with as the eluent and polystyrene as the standards, on an Agilent 1260 instrument coupled with an Agilent RI detector and equipped with two PL gel columns.

Fourier transform infrared spectroscopy (FT-IR). FT-IR spectra were performed on a Bruker EQUINOX55 spectrometer in the range from 4000 to 600 cm⁻¹ at a resolution of 2 cm⁻¹ and 32 times for each test.

Transmission electron microscope (TEM). TEM images were collected on JEOL 200EX (Tokyo, Japan) operated at 120 kV and photomicrographs were recorded using an ANT camera at calibrated magnification. 5 uL of polymersome dispersions (concentration ~ 0.6 mg/mL) were deposited onto the grid for 1 min. The grid was blotted with filter paper and immersed in 2.5 wt% phosphotungstic acid aqueous solution for 40 s for negative staining. After 5 minutes, quickly remove excess staining solution with a piece of filter paper and dry the sample naturally for TEM testing.

Dynamic light scattering (DLS). DLS was used to determine the hydrodynamic diameter (D_h) and polydispersity of the vesicle structure formed by PTMC-*b*-PBMA in aqueous solution, and measurements were performed using a nanoparticle size and Zeta

potential analyzer (Nanozs 90). Before testing DLS, the two block amphiphilic polymers were mixed into a solution of 0.1 mg/mL using DI water as a solvent, followed by ultrasound for 30 minutes to fully disperse the sample in the solution, followed by DLS testing. Analyze all solutions using a glass sample cell.

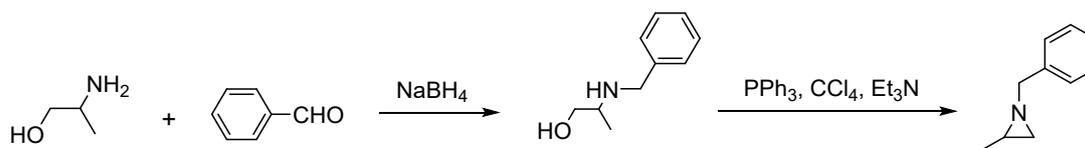
Differential scanning calorimetry (DSC). DSC analysis of the samples were performed on a NETZSCH DSC 206 equipment, and heated from -30 to 100 °C at a scanning rate of 10 °C min^{-1} under a constant nitrogen flow.

Thermo-gravimetric analysis (TGA). Thermal stability of TGA of samples were carried on a Mettler-Toledo TGA/SDTA851e in the range from 25 to 600 °C at a heating rate of 10 °C min^{-1} under a constant nitrogen flow.

2. Experimental section.

1) Synthesis of Aziridine.

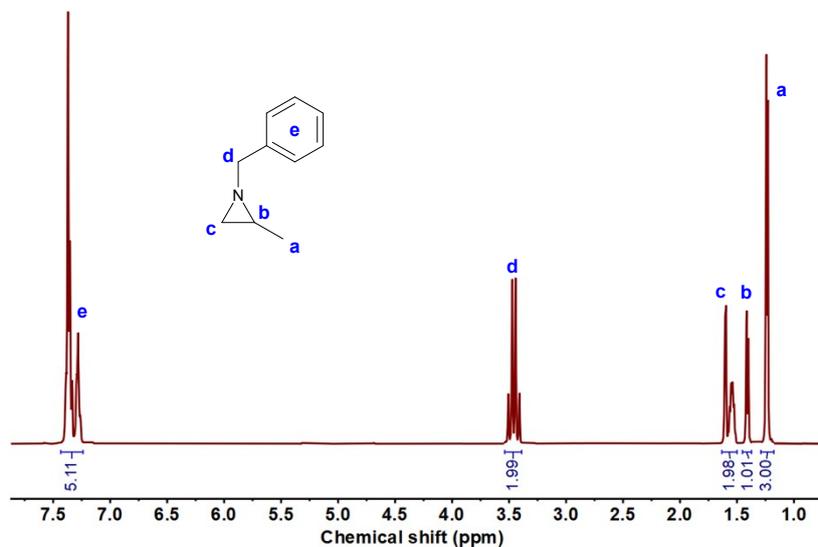
The aziridine derivatives were synthesized by the intramolecular cyclization reaction of corresponding α -amino-alcohol according to the reported method.¹



Scheme S1 Synthesis of Aziridine.

BMA: DL-Alaninol (19.3 mL, 0.25 mol) and Benzaldehyde (30.5 mL, 0.3 mol) were added into a 250 mL round-bottom flask under an atmosphere of nitrogen. The solution was stirred at 120 °C for 6 h. Cooling reaction solution to room temperature, followed by the addition of methanol (100 mL) and stirred until homogeneous. Sodium borohydride (5.7 g, 0.15 mol) was slowly added with an ice bath. The crude product was purified using extraction method to yield 2-(benzylamino)propan-1-ol (white solid, 65% yield). Then triphenylphosphine (30.0 g, 114 mmol), 2-(benzylamino)propan-1-ol (16.5 g, 110 mmol), carbon tetrachloride (15.4 mL, 100 mmol) and triethylamine (10.1 mL, 100 mmol) were added into a 250 mL round-bottom flask, followed by the addition of acetonitrile (80 mL) to form a solution. The flask was placed into an ice bath and the reaction was examined by TLC. After 16 h, the reaction was stopped. Acetonitrile was removed by vacuum, then 300 mL *n*-hexane was poured into the yellow solid. The system was stirred vigorously for 30 min, then the white powder was filtered and the

n-hexane solution was collected. After the removal of *n*-hexane by vacuum, colorless liquid was obtained as the crude product (yellowish liquid, 60% yield). The purified BMA was obtained from the crude product by distillation. ¹H NMR (400 MHz, CDCl₃) δ 7.45 – 7.22 (m, 5H), 3.54 – 3.37 (m, 2H), 1.66 – 1.49 (m, 2H), 1.41 (dd, *J* = 6.4, 1.7 Hz, 1H), 1.24 (dd, *J* = 5.5, 1.7 Hz, 3H).



2) General procedure for the copolymerization of BMA with TMC.

PBMA-*b*-PTMC: In a glovebox, ZnCl₂ (20 μL, 0.02 mmol, 2 equiv) and MTBD (1.3 mg, 0.01 mmol, 1 equiv) was added into a flame-dried 10 mL flask equipped with a magnetic stirrer. TMC (102 mg, 1 mmol, 100 equiv) and BMA (147 mg, 1 mmol, 100 equiv) was added subsequently. The vial was removed from the glovebox, and placed in an oil bath preheated to 70 °C. After the reaction finished, the vial was removed from the oil bath, the mixture was dissolved in Dichloromethane (DCM), and a small aliquot was analyzed by ¹H NMR for conversion. Then the mixture was then dissolved in DCM and precipitated into an excess of methyl alcohol. This process was repeated three times and resultant copolymers were obtained by vacuum-drying.

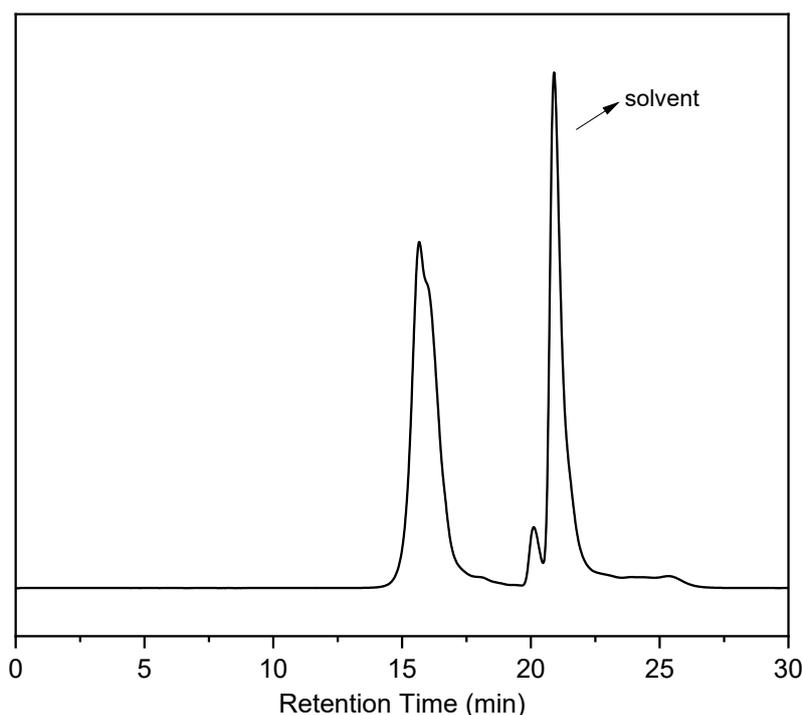


Figure S1 GPC spectra of PBMA-*b*-PTMC block copolymers catalyzed by ZnCl₂/MTBD.

3) Monitoring the copolymerization with ¹H NMR.

In an argon-filled glovebox, eight flame-dried 10 mL Schlenk bottles were prepared and charged with the same feed ratio, which is ZnCl₂ (0.02 mmol, 2 equiv), MTBD (0.01 mmol, 1 equiv), TMC (1 mmol, 100 equiv) and BMA (1 mmol, 100 equiv). The reactors were sealed and then taken out of the glovebox and stirred at 70 °C to initiate the polymerization. At a specific time, a reactor was taken out of the oil bath and quickly cooled down in an ice bath. A few reaction liquid was taken for GPC and NMR analysis.

4) Monitoring the copolymerization with in-situ IR.

The in-situ IR tracking experiments were carried out in a neat Schlenk bottle equipped with a magnet stirrer and charged with corresponding ZnCl₂ (0.02 mmol, 2 equiv), MTBD (0.01 mmol, 1 equiv), TMC (1 mmol, 100 equiv) and BMA (1 mmol, 100 equiv). Then, under nitrogen protection, insert the probe into the infrared reaction bottle and immediately start stirring at 70 °C. Click the start button on the testing interface, and the probe will scan and collect infrared signals every 15 seconds until the reaction reaches the set time and stops. The intensity of the peak at 1160 cm⁻¹, which is the stretch vibration of C-N in copolymer and 1748 cm⁻¹, which is the stretch vibration of C=O in copolymer, were monitored.

5) Synthesis of polysome.

(1) Protonation of PBMA-*b*-PTMC

Taking **P1** for example: PTMC-*b*-PBMA (**P1**, 0.095 g) was added in to a 50 mL round-bottom flask and dissolved with THF (3 mL). HCl solution (0.2 mL, 2M in DI water) was dropwise added to the solution and the solution was stirred at room temperature for 30 minutes, accompanied with white solids precipitating from the solution, *i.e.*, acidified **P1** (**AP1**). The collected white precipitates were washed with THF (5 mL) and filtered. This process was repeated for 2–3 times. After that, the white precipitates were dried in vacuum at 80 °C, and stored for use.

(2) Sample preparation for TEM test and self-assembly of amphiphilic copolymer: a solution of **AP1** (2 mg in 1mL anhydrous ethanol) was slowly dropped into DI water (anhydrous ethanol/DI water=1/2, volume ratio). After sonicating for 5 minutes, the solution was let stand for 24 hours before TEM characterization.

3. Outputs of the copolymerization of BMA and TMC mediated by various Lewis Acids in the absence or presence of Lewis base.

Table S1 Outcomes of the copolymerization of 1-benzyl-2-methylaziridine (BMA) and trimethylene carbonate (TMC) mediated by various LA/MTBD.^a

Entry	Catalyst	t (h)	Conv. ^b (%)		M_n^c (kg·mol ⁻¹)	\bar{D}^c (M_w/M_n)
			BMA	TMC		
1	AlCl ₃ /MTBD	12	<1	>99	11.1	11.1
2	FeCl ₃ /MTBD	12	<1	96	1.50	1.50
3	InCl ₃ /MTBD	12	<1	97	5.9	5.9
4	YCl ₃ /MTBD	12	<1	98	1.32	1.32
5	BEt ₃ /MTBD	16	80	<1	3.2	1.01
6	BF ₃ ·Et ₂ O/MTBD	4	99	<1	14.3	1.45
7	B(C ₆ F ₅) ₃ /MTBD	4	99	<1	13.6	1.07
8	Et ₃ O ⁺ BF ₄ ⁻ /MTBD	4	99	<1	13.2	1.17

^aGeneral conditions: the polymerizations conducted under 70 °C, LA/MTBD/TMC/BMA=2/1/100/100. ^bThe conversion of monomer, calculated by ¹H NMR in CDCl₃ using integrals of the characteristic signals. ^cDetermined by GPC in THF.

Table S2 Further study of TMC/BMA copolymerization.^a

Entry	Catalyst	t (h)	Conv. ^b (%)		M_n^c (kg·mol ⁻¹)	\bar{D}^c (M_w/M_n)
			BMA	TMC		
1	ZnCl ₂ /MTBD	8	<1	--	--	--
2	ZnCl ₂ /MTBD	1	--	92	5.7	1.36
3	ZnCl ₂ /MTBD	1	50	51	8.1	1.21
4	ZnCl ₂ /--	0.5	99.0	89	7.8	1.26
5	ZnCl ₂ /--	1	10	--	2.5	1.51
6	ZnCl ₂ /--	1	--	13	2.2	1.14
7	--/MTBD	2	<1	98	4.8	1.14
8	--/MTBD	1	--	98	8.5	1.68
9	--/MTBD	1	<1	--	--	--

^aGeneral condition: All reactions were performed with ZnCl₂/MTBD/TMC/BMA = 2/1/100/100 under 70 °C; ^bThe conversion of monomers determined by ¹H NMR using characteristic signals. ^cDetermined by GPC in THF and calibrated with polystyrene.

4. ¹H NMR spectra of BMA/TMC copolymer synthesized from the copolymerization mediated by ZnCl₂.

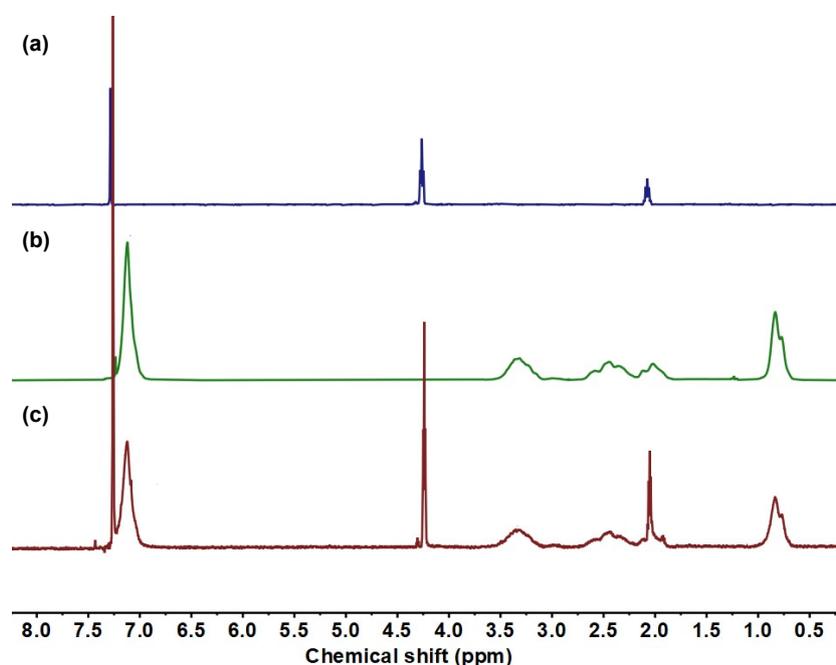


Figure S2 ¹H NMR spectra (400 MHz, CDCl₃) of (a) PTMC; (b) PBMA; (c) BMA/TMC copolymer synthesized from the copolymerization mediated by ZnCl₂.

5. ¹³C NMR spectra of PBMA, (rac)-BMA/TMC copolymer, and (S)-

BMA/TMC copolymer

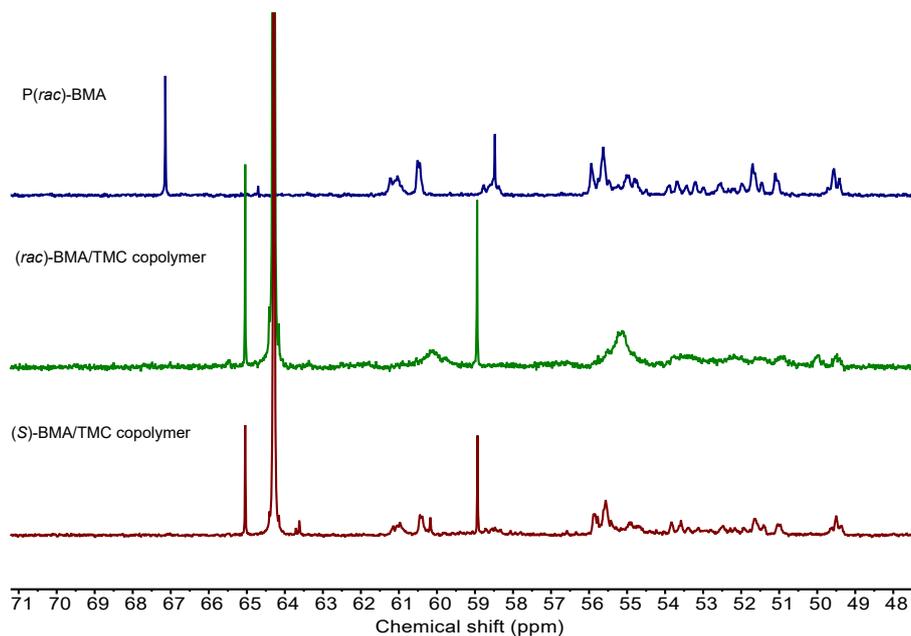


Figure S3 ^{13}C NMR of PBMA (top), (*rac*)-BMA/TMC copolymer (middle), and (*S*)-BMA/TMC copolymer (bottom).

6. HSQC spectra of (*S*)-BMA/TMC copolymer.

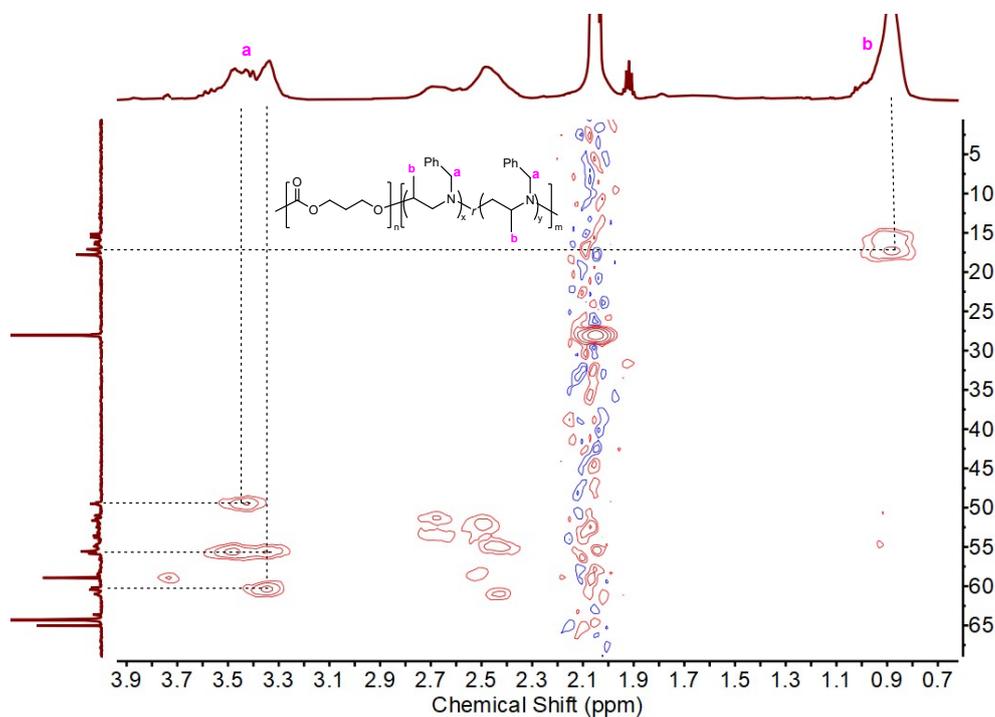


Figure S4. HSQC spectra of (*S*)-BMA/TMC copolymer.

7. In-situ IR results of BMA/TMC copolymer synthesized from the

copolymerization mediated by ZnCl₂/MTBD.

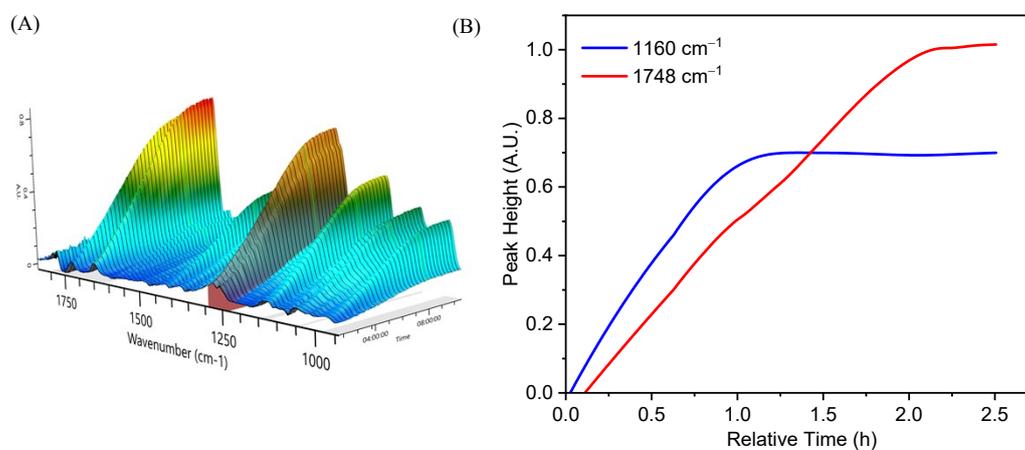


Figure S5. (A) Three-dimensional stack plot of the infrared spectrum of the ROCOP of BMA and TMC catalyzed by ZnCl₂/MTBD and (B) In-situ IR trace of 1160 cm⁻¹ (stretch vibration of C-N in copolymer); 1748 cm⁻¹ (stretch vibration of C=O in copolymer).

8. ¹H DOSY NMR spectra of BMA/TMC copolymer synthesized from the copolymerization mediated by ZnCl₂.

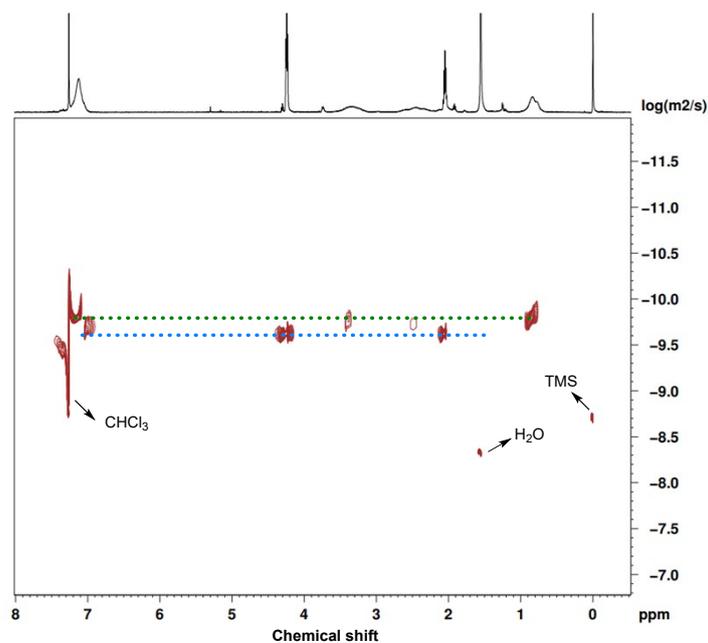


Figure S6. ¹H DOSY NMR spectra of the polymer catalyzed by ZnCl₂.

9. DSC curves of copolymers.

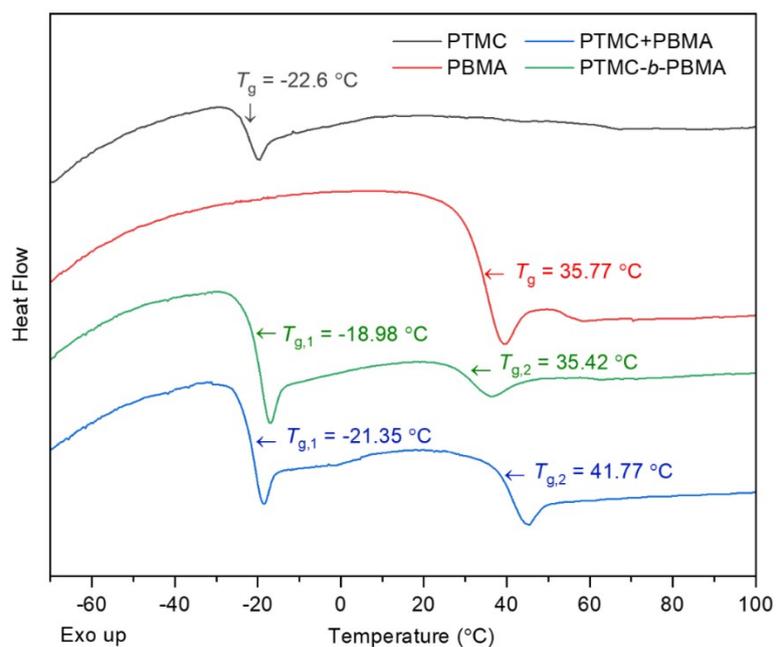


Figure S7. DSC curves of PTMC/PBMA/PBMA+PTMC/PBMA-*b*-PTMC.

10. TGA curves of copolymers.

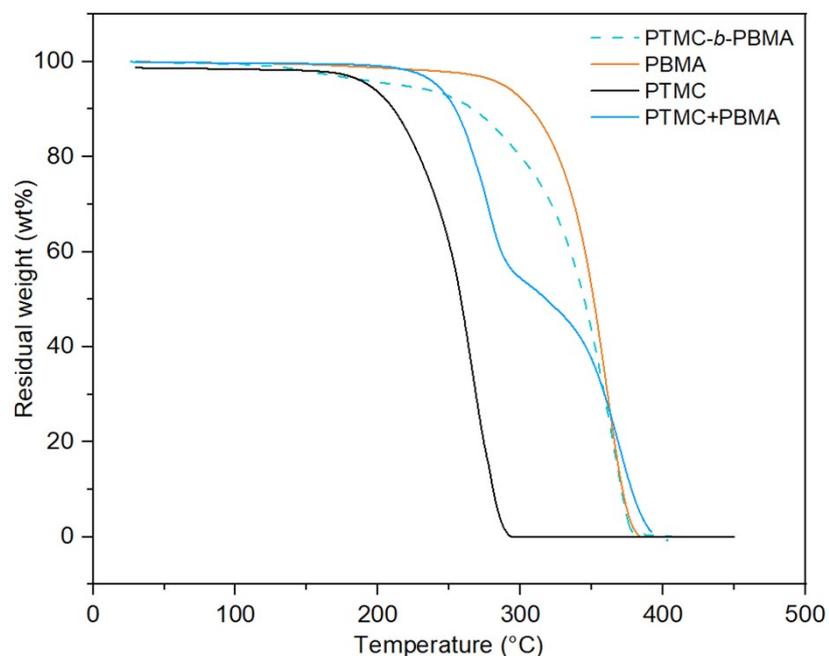


Figure S8. TGA curves of PTMC/PBMA/PBMA+PTMC/PBMA-*b*-PTMC.

11. ¹H NMR spectra of PBMA-*b*-PTMC block copolymers with different PBMA contents.

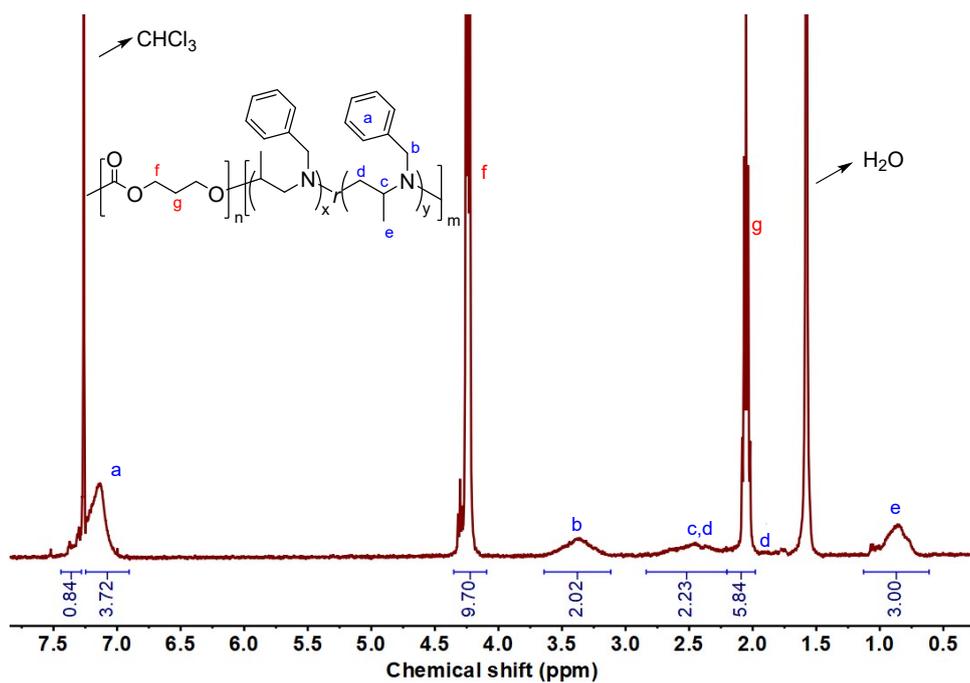


Figure S9. ¹H NMR spectra (400 MHz, CDCl₃) of the copolymer from TMC/BMA/ZnCl₂/MTBD = 200/100/2/1 (**P1**).

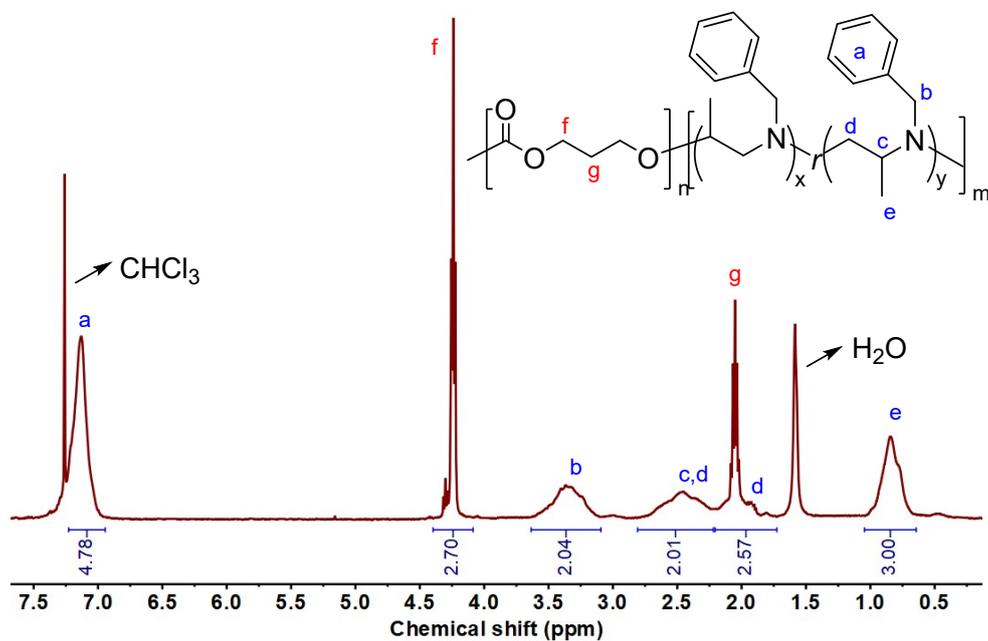


Figure S10. ¹H NMR spectra (400 MHz, CDCl₃) of the copolymer from TMC/BMA/ZnCl₂/MTBD = 100/200/2/1 (**P2**).

12. References.

1 R. Appel. *Angew. Chem. Int. Ed.*, 1975, **14**, 801.