

## Supporting Information

# From Drug to Adhesive: A New Application of Poly(Dihydropyrimidin-2(1H)-one) via Biginelli Polycondensation

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## Experimental Section

### 1. Materials

2-(2-(2-Chloroethoxy)ethoxy)ethanol (Ouhe, 97%), 4-hydroxybenzaldehyde (Ouhe, 98%), 3,4-dihydroxybenzaldehyde (Ouhe, 98%), 4-methyleneoxetan-2-one (Ouhe, 98%), trimethylamine (Ouhe,  $\geq 99.0\%$ ), sodium iodide (NaI, Heowns, 99%), terephthalic acid (PTA, Heowns, 99%) and triethylene glycol (TEG, Heowns, 99%)

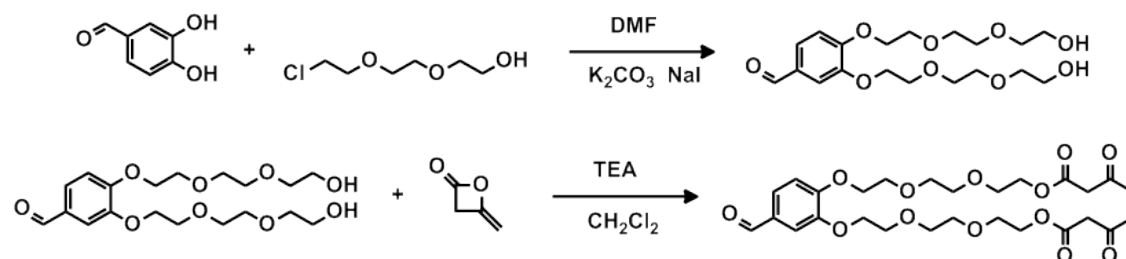
were used as purchased. 5,5'-methylenebis(2-hydroxybenzaldehyde) was synthesized as previous literatures.<sup>1</sup>

## 2. Instrumental Analysis

Gel permeation chromatography (GPC) analyses of polymers were performed using N,N-dimethyl formamide (DMF) containing 50 mM LiBr as the eluent. The GPC system was a Shimadzu LC-20AD pump system consisting of an auto injector, a MZ-Gel SDplus 10.0  $\mu\text{m}$  guard column ( $50 \times 8.0$  mm,  $10^2$  Å) followed by a MZ-Gel SDplus 5.0  $\mu\text{m}$  bead-size column ( $50 - 10^6$  Å, linear) and a Shimadzu RID-10A refractive index detector. The system was calibrated with narrow molecular weight distribution polystyrene standards ranging from 200 to  $10^6$  g mol<sup>-1</sup>. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were obtained using a JEOL JNM-ECA400 (400MHz) spectrometer for all samples. The ESI-MS data were collected using a Micro TOF-QII Bruker. The FT-IR spectra were made in a transmission mode on a Perkin-Elmer Spectrum 100 spectrometer (Waltham, MA, USA). Different scanning calorimetry (DSC) was performed using TA instruments Q2000 operated at a scanning rate of 10 °C/min. The thermal stability was measured with a TA-Q50 TGA under air atmosphere. The tensile shear strength data were collected using a microcomputer control electronic universal testing machine (MTS SYSTEMS (China) CO., LTD). Single-Molecule Force Spectroscopy (SMFS) measurements were carried out utilizing a commercially available molecular force probe 3D (Asylum Research, Santa Barbara, CA).

## 3. Monomer syntheses

### 3.1. Synthesis of monomer AB<sub>2</sub>:



3,4-Dihydroxybenzaldehyde (1.38 g, 10 mmol) was dissolved with 2-(2-(2-

chloroethoxy)ethoxy) ethanol (3.71 g, 22 mmol) in 10 mL of dry DMF. Potassium carbonate (5.52 g, 40 mmol) and sodium iodide (3.0 g, 20 mmol) were added to the mixture. The system was stirred at 110 °C for 8 h. After removing most of the solvents by rotavapor, 50 mL of water was added and the mixture was extracted by CH<sub>2</sub>Cl<sub>2</sub> three times. The organic layer was dried over MgSO<sub>4</sub> and then evaporated to get a brown oil followed by dissolved with trimethylamine (3.03 g, 30 mmol) in 15 mL of CH<sub>2</sub>Cl<sub>2</sub>. 4-Methyleneoxetan-2-one (1.85 g, 22 mmol) was added to the mixture slowly with rapidly stirring at room temperature. Then, the system was stirred at 40 °C for 6 h. After removing the solvents, the residue was dissolved in 25 mL of ethyl acetate and washed by diluted hydrochloric acid (0.1 M) and saturated sodium chloride solution three times. The organic layer was dried over MgSO<sub>4</sub> and then evaporated to get the product as an orange oil (5.1 g, 89.4%).

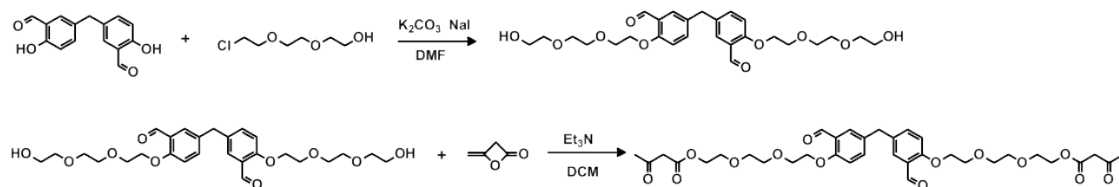
<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>, δ/ppm): 9.78 (s, 1H, CHO), 7.49 (d, 1H, *J* = 8.2 Hz, CHCHCCHO), 7.39 (s, 1H, CCHCCHO), 7.14 (d, 1H, *J* = 8.2 Hz, CHCHCCHO), 4.09-4.20 (m, 8H, CH<sub>2</sub>OAr, CH<sub>2</sub>OCO), 3.47-3.77 (m, 20H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>O, COCH<sub>2</sub>CO), 2.13 (s, 6H, COCH<sub>3</sub>).

<sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>, δ/ppm): 201.96, 191.80, 167.76, 154.22, 148.97, 130.26, 126.45, 113.14, 112.15, 70.52, 70.32, 69.22, 68.85, 68.69, 64.31, 50.00, 30.39.

IR (ν/cm<sup>-1</sup>): 2873, 1738, 1714, 1685, 1585, 1509, 1266, 1046, 948, 866, 810.

ESI-MS: observed (expected): 593.2203 (593.2205) [M+Na<sup>+</sup>].

### 3.2. Synthesis of monomer A<sub>2</sub>B<sub>2</sub>:



5,5'-Methylenebis(2-hydroxybenzaldehyde) (2.56 g, 10 mmol) was dissolved with 2-(2-(2-chloroethoxy)ethoxy) ethanol (3.71 g, 22 mmol) in 10 mL of dry DMF. Potassium carbonate (5.52 g, 40 mmol) and sodium iodide (3.0 g, 20 mmol) were added to the mixture. The system was stirred at 110 °C for 8 h. After removing most

of the solvents by rotavapor, 50 mL of water was added and the mixture was extracted by CH<sub>2</sub>Cl<sub>2</sub> three times. The organic layer was dried over MgSO<sub>4</sub> and then evaporated to get a brown oil followed by dissolved with trimethylamine (3.03 g, 30 mmol) in 15 mL of CH<sub>2</sub>Cl<sub>2</sub>. 4-Methyleneoxetan-2-one (1.85 g, 22 mmol) was added to the mixture slowly with rapidly stirring at room temperature. Then, the system was stirred at 40 °C for 6 h. After removing the solvents, the residue was dissolved in 25 mL of ethyl acetate and washed by diluted hydrochloric acid (0.1 M) and saturated sodium chloride solution three times. The organic layer was dried over MgSO<sub>4</sub> and then evaporated to get the product as an orange oil (6.2 g, 90.0%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, δ/ppm): 10.33 (s, 2H, CHO), 7.47 (s, 2H, CHCCHO), 7.21 (d, 2H, *J* = 8.5 Hz, CHCCO), 6.82 (d, 2H, *J* = 8.5 Hz, CHCCH<sub>2</sub>), 4.07-4.20 (m, 8H, CH<sub>2</sub>OAr, CH<sub>2</sub>OCO), 3.50-3.80 (m, 20H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>O, COCH<sub>2</sub>CO), 3.37 (s, 2H, ArCH<sub>2</sub>Ar), 2.12 (s, 6H, COCH<sub>3</sub>).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, δ/ppm): 200.64, 189.75, 167.14, 159.91, 136.36, 133.41, 127.97, 124.86, 113.38, 70.85, 70.56, 69.50, 68.90, 68.38, 64.26, 49.91, 39.66, 30.14.

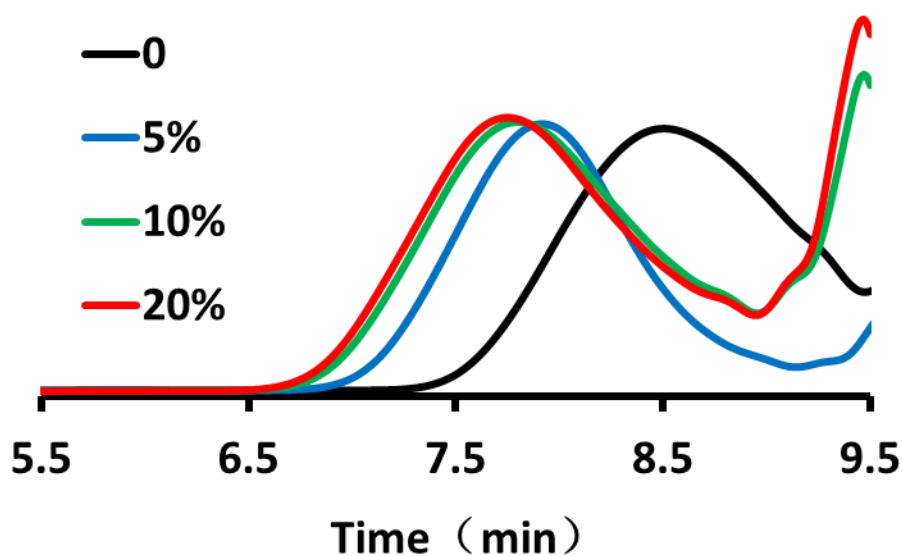
IR (ν/cm<sup>-1</sup>): 2872, 1737, 1713, 1681, 1495, 1243, 1046, 931, 812, 734.

ESI-MS: observed (expected): 711.2619 (711.2623) [M+Na<sup>+</sup>].

## 4. Polymerization

### 4.1. Biginelli polycondensation with different amount of catalyst

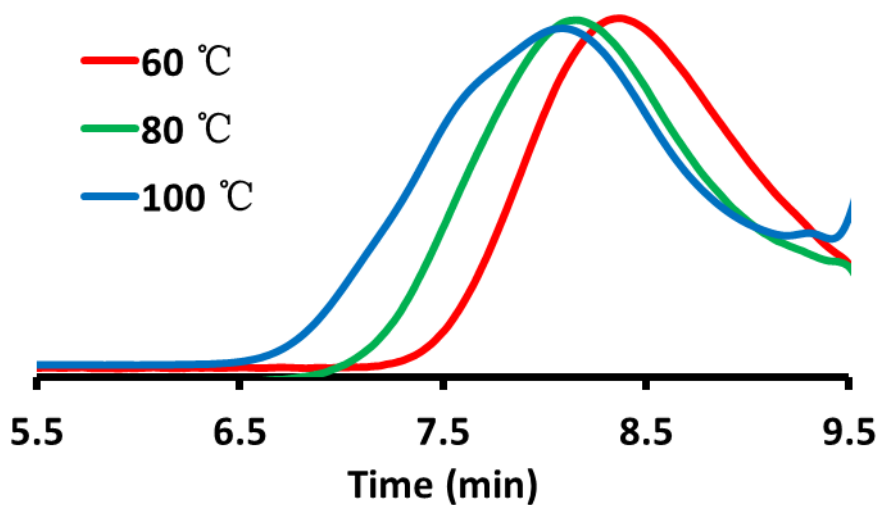
Monomer AB (338 mg, 1 mmol) was dissolved with urea (120 mg, 2 mmol) in acetic acid (0.5 mL) in four tubes. Then different amount of magnesium chloride (0, 5%, 10%, 20%) was added to the mixture, respectively. The system was stirred at 100 °C for 1 h. Samples were taken for GPC analyses for molecular weight determination. From the result, Biginelli polycondensation can also smoothly proceed under catalyst free condition with a slower rate (**Fig. S1**).



**Fig. S1.** GPC tracking of Biginelli polycondensation with different amount of catalyst (100 °C, 1 h).

#### 4.2. Biginelli polycondensation at different temperature

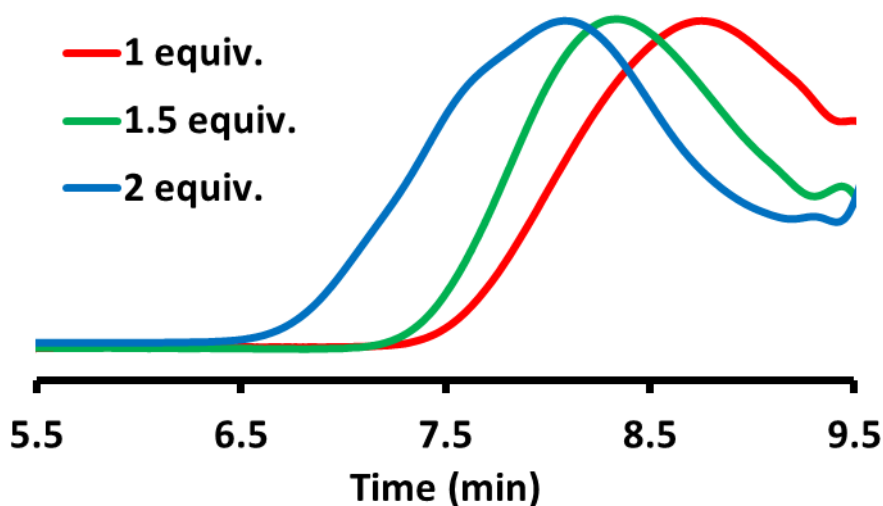
Monomer AB (338 mg, 1 mmol) was dissolved with urea (120 mg, 2 mmol) and magnesium chloride (9.5 mg, 0.1 mmol) in acetic acid (0.5 mL) in three tubes. The system was stirred at different temperature (60 °C, 80 °C, 100 °C) for 1 h, respectively. Samples were taken for GPC analyses for molecular weight determination, and the Biginelli polycondensation was found to be accelerated under higher temperature (Fig. S2).



**Fig. S2.** GPC tracking of Biginelli polycondensation at different temperature.

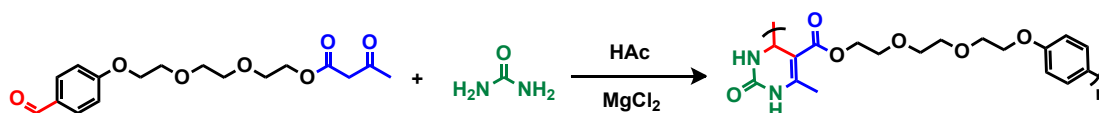
### 4.3. Biginelli polycondensation with different amount of urea

Monomer AB (338 mg, 1 mmol) was dissolved with different amount of urea (60 mg, 1 mmol, 90 mg, 1.5 mmol, 120 mg, 2 mmol) and magnesium chloride (9.5 mg, 0.1 mmol) in acetic acid (0.5 mL) in three tubes. The system was stirred at 100 °C for 1 h, respectively. Samples were taken for GPC analyses for molecular weight determination, and the Biginelli polycondensation was found to be accelerated with more urea (**Fig. S3**).

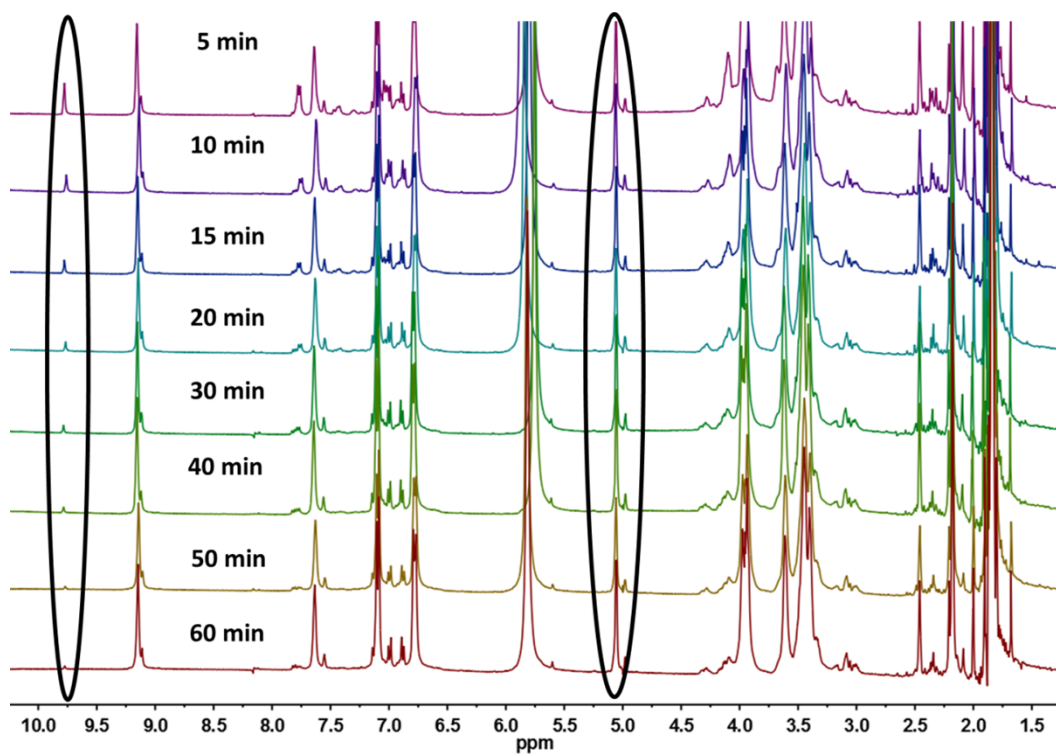


**Fig. S3.** GPC tracking of Biginelli polycondensation with different amount of urea (100 °C, 1 h).

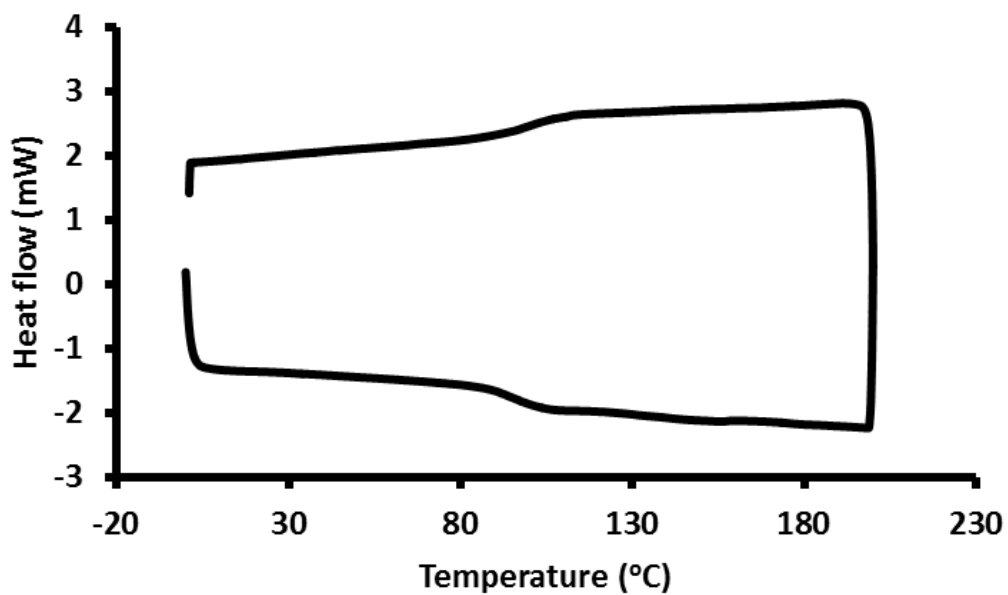
### 4.4. Large scale preparation of poly(DHPMs) in solvent



Monomer AB (10.1 g, 30 mmol) was dissolved with urea (3.6 g, 60 mmol) in acetic acid (15 mL). Then magnesium chloride (0.28 g, 3 mmol) was added to the mixture. The system was stirred at 100 °C for 4 h. Samples were taken periodically for <sup>1</sup>H NMR (**Fig. S4**) and GPC analyses for conversion and molecular weight determination, respectively. The final polymer was simply purified by precipitation into cold water and washed for 3 times by water and diethyl ether. The glass transition ( $T_g$ ) of the pure polymer was tested as 96.5 °C (**Fig. S5**) and the degradation temperature is about 300 °C (**Fig. S6**).



**Fig. S4.** <sup>1</sup>H NMR analysis (DMSO-d<sub>6</sub>, 400 MHz) of the crude of the condensation polymerization of monomer AB and urea.



**Fig. S5.** DCS traces for both heating/cooling (rate of 10 °C/min) of poly(DHPMs).

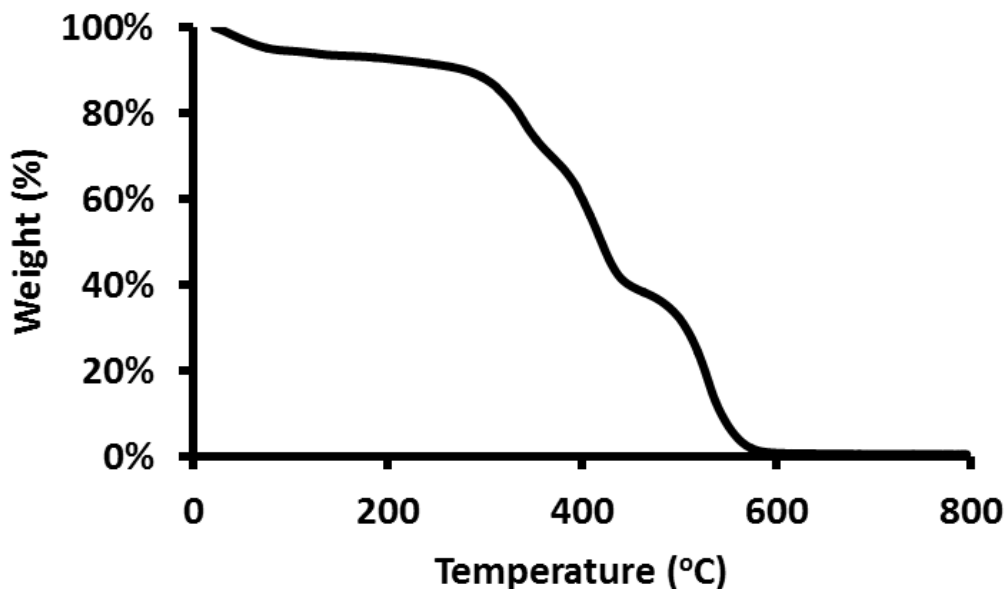


Fig. S6. TGA curve of poly(DHPMs).

#### 4.5. Quick neat Biginelli polycondensation of monomer AB under heat

Urea was added on glass surface, and then covered with the monomer AB, equal amount of monomer AB was dropped on the other zone on same glass as the control. Both zones were heated by an electric heat gun simultaneously for 30 seconds.  $^1\text{H}$  NMR spectrum of the control group was tested and no any polymerization was observed (Fig. S7).

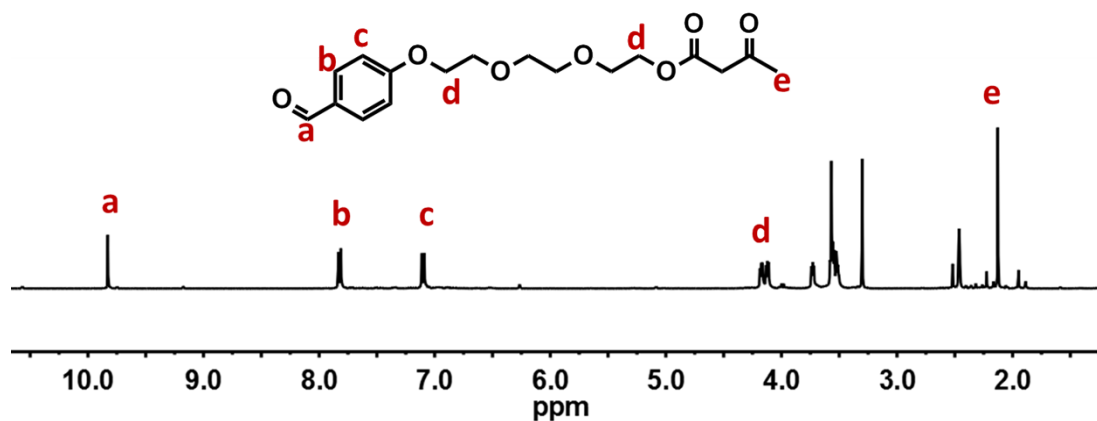
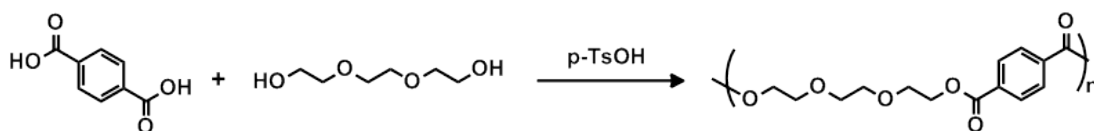


Fig. S7.  $^1\text{H}$  NMR analysis (DMSO- $d_6$ , 400 MHz) of the control group.

#### 4.6. Synthesis of polyester with terephthalic acid and triethylene glycol





Terephthalic acid (1.66 g, 10 mM) and triethylene glycol (1.50 g, 10 mM) were added in schlenk tube and p-toluenesulfonic acid (0.17 g, 1 mM) was as catalyst. The system was stirred under vacuum to remove water and kept at 150 °C for 48 h. The final polymer was simply purified by by fractional precipitation into cold diethyl ether/THF and washed for 3 times by diethyl ether to get the product as a yellow oil (2 g, 71%,  $M_{n\text{GPC}}\sim 27700$ , PDI~1.18).

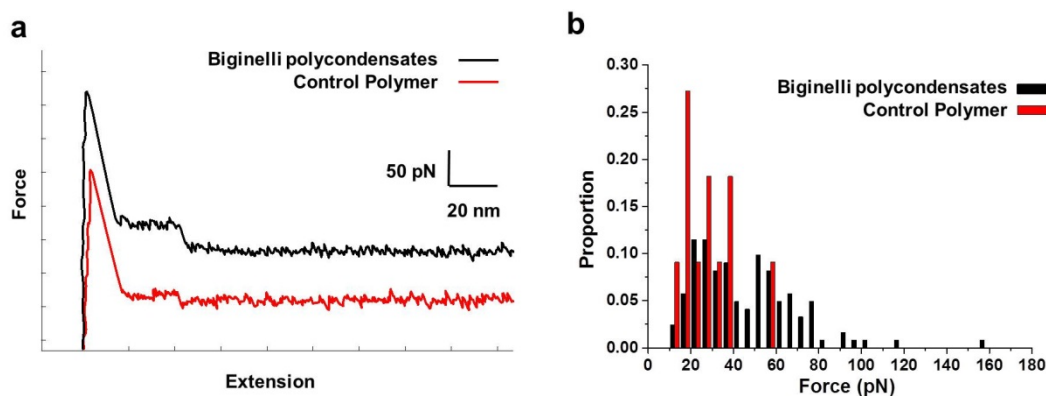
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ,  $\delta/\text{ppm}$ ): 7.82~8.20 (m, 4H, Ph), 4.07-4.20 (m, 8H,  $\text{CH}_2\text{OAr}$ ,  $\text{CH}_2\text{OCO}$ ), 4.27-4.53 (m, 4H,  $\text{CH}_2\text{OOCPhCOOCH}_2$ ), 3.50-3.90 (m, 8H,  $\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{O}$ ).

#### 4.7 The SMFS experiment

The details of SMFS experiment have been described elsewhere.<sup>2</sup> In brief, when an AFM tip (spring constant: 0.010-0.040 N/m) is brought into contact with an gold substrate, the polymer absorbed onto the gold substrate ahead of the time have chance to absorb onto the AFM tip. When the tip is separated from the substrate, the polymer chain will be desorbed gradually from the substrate, resulting in the bending of AFM tip. The bending extent of the AFM tip were recorded and converted to force curves, which can offer information about the interaction between the polymer chain and the substrate.

The representative force curves of desorption of Biginelli polycondensates and the control polymer (polyester counterpart, sharing the same chemical structure with Biginelli polycondensates except the DHMPs structure part) from the gold surface (**Fig S8a**), both of them have the same characteristic shape of a long flat plateau, corresponding to the continuous desorption process of polymer chain from the gold substrate. The heights of the plateaus represent the desorption forces. The statistically analyses to the heights of all hundreds of plateaus are shown in **Fig S8b**. We can see clearly that both Biginelli polycondensates and the control polymer get the same kinds

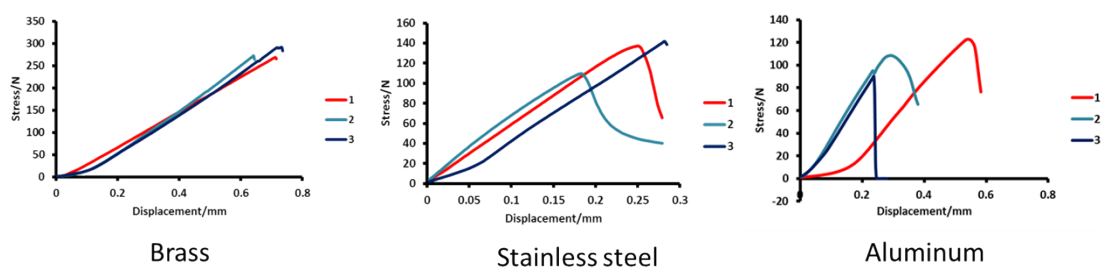
of plateaus at 10-40 pN, which corresponding to the adsorption driven by common unspecific interaction. However, Biginelli polycondensates have much more possibility to get plateaus with higher force, showing that the DHMPs structure might has specific interaction stronger than common adsorption with the gold surface.



**Fig. S8.** a) Representative force curves of desorption of Biginelli polycondensates (black) and the control polymer (red) from the gold surface. b) The statistically analyses to the heights (forces) of all the plateaus of Biginelli polycondensates (black) and the control polymer (red) respective.

#### 4.8. Metal bonding with the Biginelli polycondensation of monomer AB

Tensile shear strength was tested by a microcomputer control electronic universal testing machine to evaluate the bonding effect of different metals. The force increases with the increasing of displacement, and when the two metal sheets separate, the test stops. Three measurements were performed (different color lines in Fig. S9) and the results were shown as the mean  $\pm$  SD,  $n = 3$  (Fig. S9).



**Fig. S9.** Tensile shear strength tests of different metals.

## Reference

1. Guieu, S.; Rocha, J.; Silva, A. *Tetrahedron* **2013**, 69, (44), 9329-9334.
2. Hugel, T.; Seitz, M. *Macromol. Rapid Commun.* **2001**, 22, 989-1016.