Supporting Information

Introducing Mecaptoacetic Acid Locking Imine Reaction into Polymer Chemistry as a Green Click Reaction

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Experimental Section

1. Materials

Mercaptoacetic acid (Alfa Aesar, 97%), methoxypolyethylene glycol (mPEG, Mn ~ 5000, Aldrich), methoxypolyethylene glycol amine (mPEG-NH₂, Mn ~2000, Aladdin, $\geq 0.4 \text{ mmol/g NH}_2$ loading), 4-formylbenzoic acid (Aladdin, 98%), N,N'dicyclohexylcarbodiimide (DCC, Aladdin, $\geq 99.0\%$), 4-dimethylamiopryidine (DMAP, Aladdin, 99%), 1,4-butylene glycol (Aladdin, $\geq 99.0\%$), 2-bromoisobutyryl bromide (Maya, 97%), 1,1,4,7,7-pentamethyldiethylenetriamine (J&K, 98%), methyl methacrylate (MMA, Aladdin 99%), terephthalaldehyde (Aladdin, $\geq 99.0\%$), hexamethylenediamine (Aladdin, $\geq 99.0\%$), 2-mercaptopropionic acid (J&K Chemical, 95%) were used as purchased. CuBr was washed by acetic acid prior to use. N-(2-aminoethyl)-5-(dimethylamino)-naphthalene-1-sulfonamide (dansyl ethylenediamine)¹, benzaldehyde terminated methoxypolyetylene glycol (mPEG- CHO, $M_{nGPC} \sim 26300$, PDI: 1.03² and 4-hydroxybutyl 2-bromo-2-methylpropanoate³ were synthesized as previous literatures.

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 μ m guard column(50 \times 8.0 mm, 10² Å) followed by a MZ-Gel SDplus 5.0 μ m bead-size column (50 - 10⁶ 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 10⁶ g mol⁻¹. ¹H NMR and ¹³C 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). UV-Visible absorption spectra were obtained on uV/Vis/NIR Perkin-Elmer lambda750 spectrometer (Waltham, MA, USA) using quartz cuvettes of 1 cm path length. The fluorescence measurements were obtained on a Perkin-Elmer LS-55 spectrometer equipped with quartz cuvettes of 1 cm path length.

3. Method

3.1. Synthesis of 4-((2-bromo-2-methylpropanoyl)oxy)butyl 4-formylbenzoate:



4-Hydroxybutyl 2-bromo-2-methylpropanoate (1.62 g 6.76 mmol) was dissolved with 4-formylbenzoic acid (1.22 g, 8.13 mmol) and DMAP (25.0 mg, 0.2 mmol) in 40 mL of dry CH_2Cl_2 and 5 mL of anhydrous THF. DCC (2.79 g, 13.5 mmol) was added to the mixture under nitrogen atmosphere. The system was stirred at 25 °C for 24 h. After removing the solvents, 15 mL of toluene was added and the insoluble white

solid was removed by filtration. The organic layer was dried over MgSO₄ before evaporated, and the residue was purified via column chromatography with silica gel eluting with ethyl acetate/petroleum ether (1/9) to get a pale yellow oil (1.86 g, 74%).

¹H NMR (400 MHz, CDCl₃, δ /ppm): 10.04 (s, 1H, C<u>H</u>O), 8.13 (d, 2H, *J* = 8.0 Hz, C<u>H</u>CCHO), 7.89 (d, 2H, *J* = 8.0 Hz, C<u>H</u>CCOO), 4.35 (t, 2H, *J* = 6.0 Hz, C<u>H</u>₂OCOAr), 4.20 (t, 2H, *J* = 6.0 Hz, C<u>H</u>₂OCOC), 1.77-1.92 (m, 10H, CH₂C<u>H</u>₂C<u>H</u>₂CH₂, CC<u>H</u>₃). ¹³C NMR (100 MHz, CDCl₃, δ /ppm): 191.83, 171.82, 165.66, 139.27, 135.29, 130.31, 129.69, 65.50, 65.16, 55.93, 30.85, 25.37. IR (v/cm⁻¹): 2961, 2854, 2734, 1722, 1705, 1463, 1378, 1268, 1201, 1161, 1104, 1015,

947, 929, 758.

ESI-MS: observed (expected): 372.0511 (371.0489) [M+H⁺].





MMA (6.0 g, 60 mmol), 4-((2-bromo-2-methylpropanoyl)oxy)butyl 4-formylbenzoate as initiator (222 mg, 0.62 mmol), CuBr (22 mg, 0.15 mmol) and 1,1,4,7,7-pentamethyldiethylenetriamine (33 μ L, 0.30 mmol) were charged into a dry Schlenk tube along with toluene (10 mL). The Schlenk tube was sealed with a rubber septum and degassed through three freeze-pump-thaw cycles flow. The tube was then put into an oil bath maintained at 65 °C for 17 hours. The crude was then precipitated from toluene to cold petroleum ether for 3 times, and then dried under vacuum to obtain the pure polymer for further use and characterizations.

¹H NMR (400 MHz, CDCl₃, δ/ppm): 10.05 (s, C<u>H</u>O), 8.14 (d, *J* = 8.0 Hz, C<u>H</u>CCHO),

7.91 (d, J = 8.0 Hz, CHCCO), 4.34 (t, CH₂OCOAr), 4.04 (m, CH₂OCOC), 3.34-3.72 (m, COOCH₃), 1.70-2.10 (m, CH₂C), 0.75-1.10 (m, CH₃C).

The polymerization conversion (60%) was calculated by ¹H NMR of the crude, comparing the peaks of the vinyl protons and the methoxy protons. The molecular weight was obtained by the methylene protons (CH₂OCOAr) on the polymers compared to the one methoxy protons (DP ~ 60, $M_{nNMR} \sim 6300$).

GPC was also tested to evaluate the PDI and molecular weight of the final polymer $(M_{nGPC} \sim 23900, PDI: 1.09)$.

3.3. Chain-end modification of mPEG-CHO:



mPEG-CHO (0.10 g, 0.02 mmol) and N-(2-aminoethyl)-5-(dimethylamino)naphthalene-1-sulfonamide (dansyl ethylenediamine) (6.3 mg, 0.02 mmol) were charged into a dry EP tube along with DMSO (200 μ L). The EP tube was put into thermo-shaker at room temperature (25 °C) for 0.25 hours. Then mercaptoacetic acid (14 μ L, 0.20 mmol) was added into the EP tube and reacted for next 1.5 hours. Samples were taken periodically for ¹H NMR analyses for conversion calculation (**Figure S1**). The mixture was simply purified by precipitation into cold ethyl ether and washed for 3 times.

¹H NMR (400 MHz, DMSO-d₆, δ /ppm): 8.44 (d, *J* = 8.0 Hz, CHCHC<u>H</u>CS), 8.19 (d, *J* = 8.0 Hz, C<u>H</u>CHCHCS), 8.05-8.13 (m, N<u>H</u>), 7.96 (d, *J* = 8.0 Hz, CHC<u>H</u>CHCS), 7.92 (d, *J* = 8.0 Hz, C<u>H</u>CCOO), 7.52-7.62 (m, C<u>H</u>C<u>H</u>CHCN), 7.37 (d, *J* = 8.0 Hz, C<u>H</u>CCHN), 7.24 (d, *J* = 8.0 Hz, CHCHC<u>H</u>CN), 5.78 (s, SC<u>H</u>N), 4.42 (t, C<u>H</u>₂OCOAr), 3.43-3.59 (m, OC<u>H</u>₂C<u>H</u>₂O), 3.23 (s, OC<u>H</u>₃), 2.82 (s, NC<u>H</u>₃). Mn_{GPC} ~26700, PDI = 1.03.

PL: $\lambda ex max = 340 \text{ nm}$, $\lambda em max = 547 \text{ nm}(Figure S2)$.

3.4. The linkage of mPEG-NH₂ and PMMA-CHO:



PMMA-CHO (126 mg, 0.02 mmol) and mPEG-NH₂ (50 mg, 0.025 mmol) were charged into a dry EP tube along with DMSO (200 μ L). The EP tube was put into thermo-shaker at room temperature (25 °C) for 0.5 hours. Then mercaptoacetic acid (10 μ L, 0.14 mmol) was added and reacted for next 1.5 hours. Samples were taken periodically for GPC and ¹H NMR analyses for molecular weight calculations (**Figure S3**) and conversion (**Figure S4**), respectively. The mixture was simply purified by precipitation into cold isopropanol and washed by petroleum ether 3 times.

¹H NMR (400 MHz, CDCl₃, δ /ppm): 8.04 (d, J = 8.0 Hz, CHCCO), 7.40 (d, J = 8.0 Hz, CHCCHN), 6.01 (s, SCHN), 4.37 (t, CH₂OCOAr), 4.09 (m, CH₂OCOC), 3.62-3.66 (m, OCH₂CH₂O), 3.58-3.62 (m, COOCH₃), 3.38 (s, OCH₃), 1.70-2.10 (m, CH₂C), 0.75-1.10 (m, CH₃C).

 $Mn_{GPC} \sim 27400$, PDI = 1.08.

3.5. Condensation polymerization of terephthalaldehyde, hexamethylenediamine and 2-mercaptopropionic acid:



Terephthalaldehyde (0.838 g, 6.25 mmol) was charged into a dry round bottom flask along with DMSO (4.0 mL). Then hexamethylenediamine (0.726 g, 6.25 mmol) in DMSO (1.0 mL) was added into terephthalaldehyde solution with rapidly stirring at room temperature (25 °C). 2-Mercaptopropionic acid (3.00 g, 25 mmol) was then quickly added into the mixture and the system was kept at 25 °C for next 48 hours.

Samples were taken periodically for ¹H NMR and GPC analyses for conversion (**Figure S5**) and molecular weight determination, respectively. The final polymer was simply purified by precipitation into cold ethyl ether and washed for 3 times.

¹H NMR (400 MHz, DMSO-d₆, δ /ppm): 7.29-7.41 (m, <u>Ph</u>), 5.66-5.78 (m, SC<u>H</u>N), 3.84-4.10 (m, C<u>H</u>CH₃), 3.30-3.61 (m, C<u>H₂</u>N), 0.80-1.50 (m, NCH₂C<u>H₂CH₂, CHCH₃). Mn_{GPC} ~18800, PDI = 1.49.</u>

Supporting Data



Figure S1. ¹H NMR analysis (DMSO-d₆, 400 MHz, portion) of the crude of chainend modification reaction after 1.5 h.



Figure S2. Fluorescence spectrum of the fluorescent group terminated mPEG.



Figure S3. GPC tracking of the generation of MALI-locked copolymer.



Figure S4. ¹H NMR analysis (DMSO-d₆, 400 MHz, portion) of the crude of MALI coupling reaction after 1.5 h.



Figure S5. ¹H NMR analysis (DMSO- d_6 , 400 MHz) of the crude of the condensation polymerization of terephthalaldehyde, hexamethylenediamine and 2-mercaptopropionic acid.

Reference

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