Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Controlled RAFT Polymerization Facilitated by Nanostructured Enzyme Mimic

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Experimental Section

Materials

N,*N*-dimethylacrylamide (DMA, Aldrich, 99%), methyl acrylate (MA, Aldrich, 99%), *N*-hydroxyethyl acrylamide (NHEA, Aldrich, 97%) and 2-(dimethylamino)ethyl methacrylate (DMAEMA, Aldrich, 98%) were passed over basic alumina to remove inhibitors prior to use. Glucose oxidase from Aspergillus niger was purchased from Sigma-Aldrich as a lyophilized powder. Glycine (Aldrich, >99%), 1,4-benzenedicarboxylate (BDC, Aldrich, 98%), iron(III) chloride hexahydrate ($FeCl_3 \cdot 6H_2O$, Aldrich, 98%), trans-2-(3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene)malononitrile (DCTB, Aldrich, >99%), sodium trifluoroacetate (NaTFA, Aldrich, 98%), D-glucose (Aldrich, 99.5%) and 3,3′,5,5′-tetramethylbenzidine (TMB) were purchased from Sigma-Aldrich and used as received. Hydrogen peroxide (H_2O_2, 30 wt%), ethanol, dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) was purchased from Chem-Supply Pty Ltd and used as received. Deuterium oxide (D_2O, 99.9%) and dimethyl sulfoxide-D6 (DMSO-d_6, 99.9%) were purchased from Cambridge Isotope Laboratories Inc. Chain transfer agents S,S'-bis(α,α'-dimethyl-α"-acetic acid)trithiocarbonate (CTA-1) was synthesized as previously reported,[1] and 4-(((2-carboxyethyl)thio)carbonothioyl)thio)-4-cyanopentanoic acid (CTA-2) was purchased from BORON MOLECULAR and used as received.

Characterization

Nuclear Magnetic Resonance (NMR) Spectroscopy. ^{1}H NMR spectroscopy was conducted on a Varian Unity 400 MHz spectrometer operating at 400 MHz, using the

deuterated solvent ($CDCl_3$) as reference and a sample concentration of approximately 10 mg·mL^{-1}.

Gel-Permeation Chromatography (GPC). The aqueous GPC system consisted of three Waters Ultrahydrogel columns in series ((i) 250 Å porosity, 6 μm bead size; (ii) and (iii) linear, 10 μm bead size). A Shimadzu RID-10 refractometer and Wyatt 3-angle MiniDawn light scattering detector were connected in series. Milli-Q water with 0.1 vol% TFA was used as eluent at a flow rate of 1 mL min^{-1} and the system operated at ambient temperature. For all polymers, dn/dc values were determined via a method of 100% mass recovery. Molecular weight and dispersity values were calculated using the Wyatt ASTRA software package from MALS data using a Debye model. When DMF was used as an eluent, the GPC analysis was conducted on a Shimadzu liquid chromatography system equipped with a Shimadzu RID-10 refractometer ($\lambda = 633$ nm) and Shimadzu SPD-20A UV-vis detector using three identical Jordi columns (5 μm bead size, Jordi Gel Fluorinated DVB Mixed Bed) in series operating at 70°C. DMF with 0.05 mol·L^{-1} LiBr (>99%, Aldrich) was employed as the mobile phase at a flow rate of 1 mL·min^{-1}. The system was calibrated using polystyrene standards. All samples were filtered through 0.45 μm nylon filters prior to injection.

Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectroscopy (MALDI-ToF MS). MALDI-ToF MS was performed on a Bruker Autoflex III mass spectrometer operating in positive-linear mode; the analyte, matrix (DCTB), and cationization agent (NaTFA) were dissolved in THF at concentrations of 10, 10, and 1 mg mL^{-1}, respectively, and then mixed in a ratio of 10:1:1. Then 0.3 μL of this solution was spotted onto a ground steel target plate, and the solvent was allowed to evaporate prior to analysis. Flex Analysis (Bruker) was used to analyze the data.

Powder x-ray diffraction (PXRD). XRD patterns of the samples were recorded on a Bruker D8 Advance instrument with Cu Ka radiation (40 kV, 40 mA) and a nickel filter, and the samples were exposed at a scanning rate of $2\theta = 0.020$ s^{-1} in the range of 5-70°.

X-ray photoelectron spectroscopy (XPS). XPS was used to confirm the change of MOF compositions. XPS was carried out on a VG ESCALAB 220i-XL spectrometer under ultra-high vacuum conditions (6×10^{-9} mbar) with a fixed photon energy (A1 Kα 1486.6 eV). A survey scan was performed between 0 and 1200 eV with a resolution of 1.0 eV and pass energy of 100 eV. High resolution scans for C 1s (281 to 293 eV), O 1s (528 to 536 eV) N 1s (396 to 405 eV) and Fe 2p (705 to 733 eV) were also conducted with a resolution of 0.05 eV and a pass energy of 20 eV.

Scanning electron microscopy (SEM). SEM was conducted on a Quanta FEG 200 ESEM. Samples were coated with gold using a Dynavac Mini Sputter Coater prior to imaging.

Atomic absorption spectroscopy (AAS). AAS measurements were conducted on a Perkin Elmer AAnalyst 400. In this study the technique is used for determining the concentration of Fe^{3+} residue leaking form MIL-53(Fe) after the removal of MOF/glycine composite through filtration.

Methods

Preparation of MIL-53(Fe) metal-organic framework. MIL-53(Fe) was synthesized according to the previous report.[2, 3] In detail, $FeCl_3 \cdot 6H_2O$ (1.08 g, 4 mmol), BDC (0.66 g, 2 mmol), and DMF (20 mL) were mixed until to obtain a yellow solution under sonication, and then the mixture was transferred to a Teflon lined stainless steel autoclave. After the autoclave was heated to 150 °C for 16 h, the obtained yellow suspension was centrifuged for 5 min at 4,400 rpm. The obtained solid was purified by a thrice treatment in ethanol and

DMF. After drying in vacuum at 50 °C overnight, a yellow power of MIL-53(Fe) was obtained.

Hydroxyl radical detection. TMB reagent has been used in this study to detect the hydroxyl radicals (which oxidise the TMB to produce the blue product ox-TMB with a λ_{max} = 652nm). Measurements were carried out in 1 mL Milli-Q water containing MOF-53(Fe) (1 mg mL^{-1}), glycine (20 mg mL^{-1}), H_2O_2 (50 mM) and TMB (500 μM) at room temperature for 5 min. The absorbance spectra were observed using a UV-vis spectrometer. In addition, absorbance of this solution at 652 nm was detected at different concentration of H_2O_2 (98, 49, 24.5, 12.3 mM) for 5 min. Finally, the relative activity of the system was determined while varying the glycine from 0 to 40 mg mL^{-1} and the MOF-53(Fe) from 0.0 to 2.0 mg mL^{-1} at an absorbance of 652 nm.

General procedure for the synthesis of polymers facilitated by peroxidase-like activity. In a 7 mL glass vial, monomer (10 mmol), 30 wt% H_2O_2 solution (0.1 mmol) and CTA (0.05 mmol) were dissolved in solvent (DI H_2O or DMSO) to give an initial monomer concentration $[M]_0$ of 5 M. $[H_2O_2]$:[CTA]:[monomer]=2:1:200. The vial was fitted with a rubber septum and sparged with Ar for 15 min. The MIL-53(Fe) (2 mg) and glycine (40 mg) were then added to the mixture under Ar protection, and the reaction mixture was stirred. Samples were taken at timed intervals via degassed syringe and immediately diluted with D_2O (or DMSO-d_6) for NMR and DI H_2O (or DMF) for GPC analysis, respectively.

Synthesis of polymers using recovered glycine/MOF composite. The applied glycine/MIL-53(Fe) composite was separated from the polymerization solution *via* centrifugation and dried in vacuum. The recovered composite were then added to a degassed solution containing DMA (10 mmol), 30 wt% H_2O_2 solution (0.1 mmol), CTA (0.05 mmol) and DI H_2O (1 mL) ($[M]_0$ = 5 M; $[H_2O_2]$:[CTA]:[DMA]=2:1:200) under Ar protection. Samples were taken via

degassed syringe and immediately diluted with D_2O for NMR and DI H_2O for GPC analysis, respectively.

In situ chain extension experiments. In a 7 mL vial glass, DMA (1.03 mL, 10 mmol), 30 wt% H_2O_2 solution (0.1 mmol,) and CTA (14.1 mg, 0.05 mmol) were dissolved in 1.03 mL DI H_2O to give an initial monomer concentration $[M]_0$ of 5 M and $[H_2O_2]$/[CTA]/[monomer] = 2/1/200. The vial was fitted with a rubber septum and sparged with Ar for 15 min. The MIL-53(Fe) (2 mg) and glycine (40 mg) were then added to the mixture under Ar protection, and the reaction mixture was stirred. After 4 hours, the monomer conversion was ≥95% by ^{1}H NMR analysis. A vial charged with 10 mmol DMA (or NHEA), 30 wt% H_2O_2 solution (8 μL) and DI H_2O (1.03 mL) was sparged with Ar for 15 min. The deoxygenated mixture was then injected into the reactor. After 4 hours, the monomer conversion was ≥98% by ^{1}H NMR analysis. Samples were also taken and diluted with DI H_2O for GPC analysis.

Polymerization of differing targeted degrees of polymerization (DP). Approach-1: To access different chain lengths, the initial molar ratio of monomer to H_2O_2 and CTA was modified. The amount of monomer (1.03 mL), MOF (2 mg) and glycine (40 mg) was fixed relative to the H_2O_2 and CTA ($[H_2O_2]$:[CTA] = 2:1). Polymer conversion in excess of 65% was observed for all cases after 4 hours, independent of the targeted DP_n's.

Approach-2: In a 50 round bottom flask, 5.15 mL DMA (50 mmol) was dissolved in DI H_2O to give an initial monomer concentration ($[M]_0$) of 1 M. The initial molar ratio of monomer to CTA (0.01 mmol for DP_n = 5000; and 0.0033 mmol for DP_n = 15000) was modified. The amount of GOx (0.08 mg), D-glucose (0.36 g), MIL-53(Fe) (2 mg) and glycine (40 mg) was fixed. Polymer conversion in excess of 75% was observed for all cases after 24 hours.

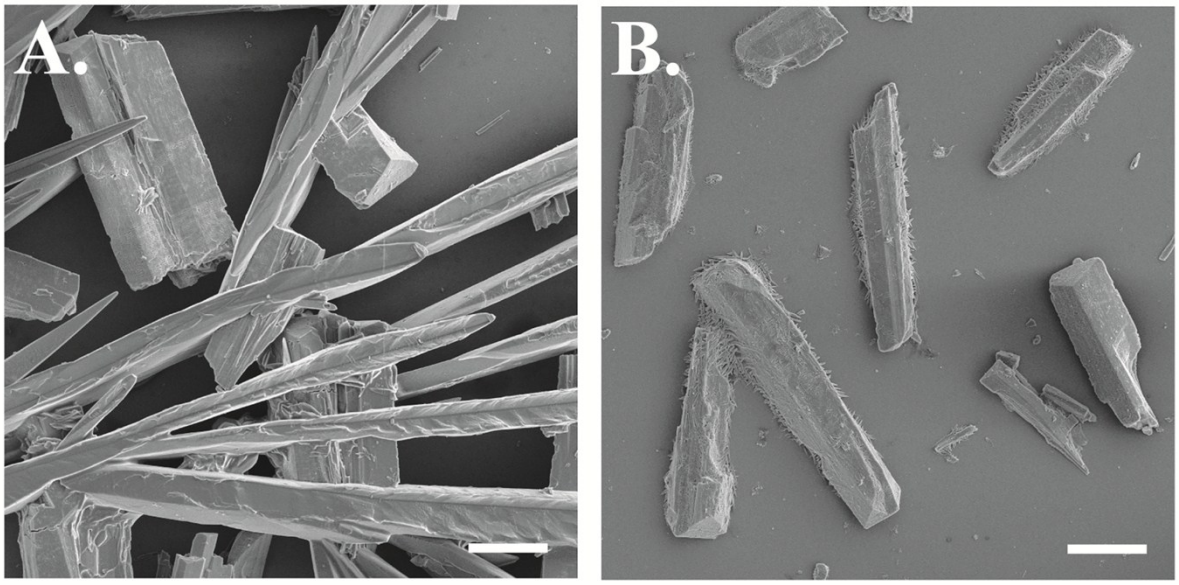

Figure S1. SEM images of (A) MIL-53(Fe) MOF and (B) glycine/MIL-53(Fe) composite. The scale bar represents 200 nm.

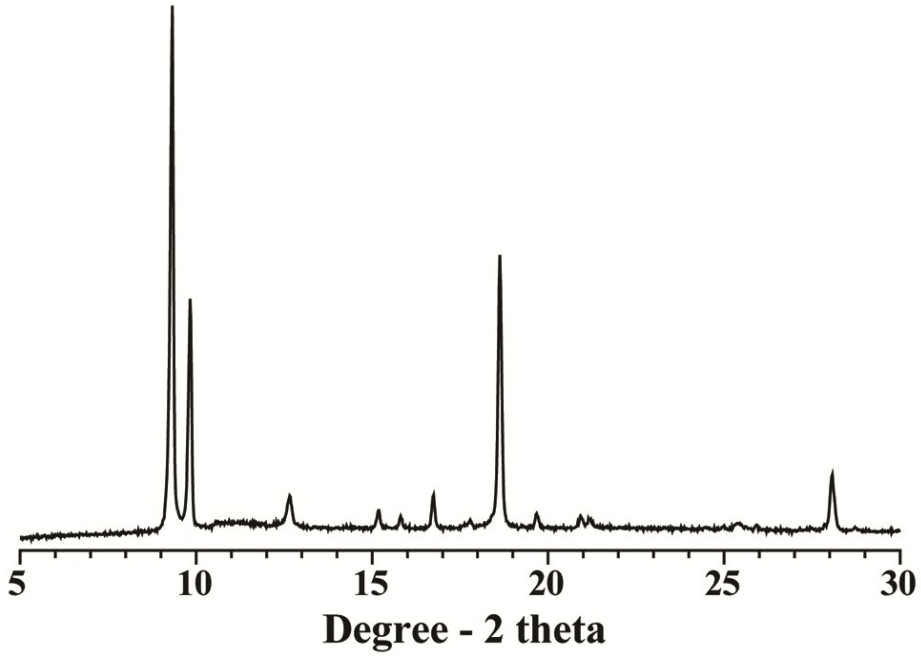

Figure S2. Powder x-ray diffraction (PXRD) pattern of MIL-53(Fe) MOFs.

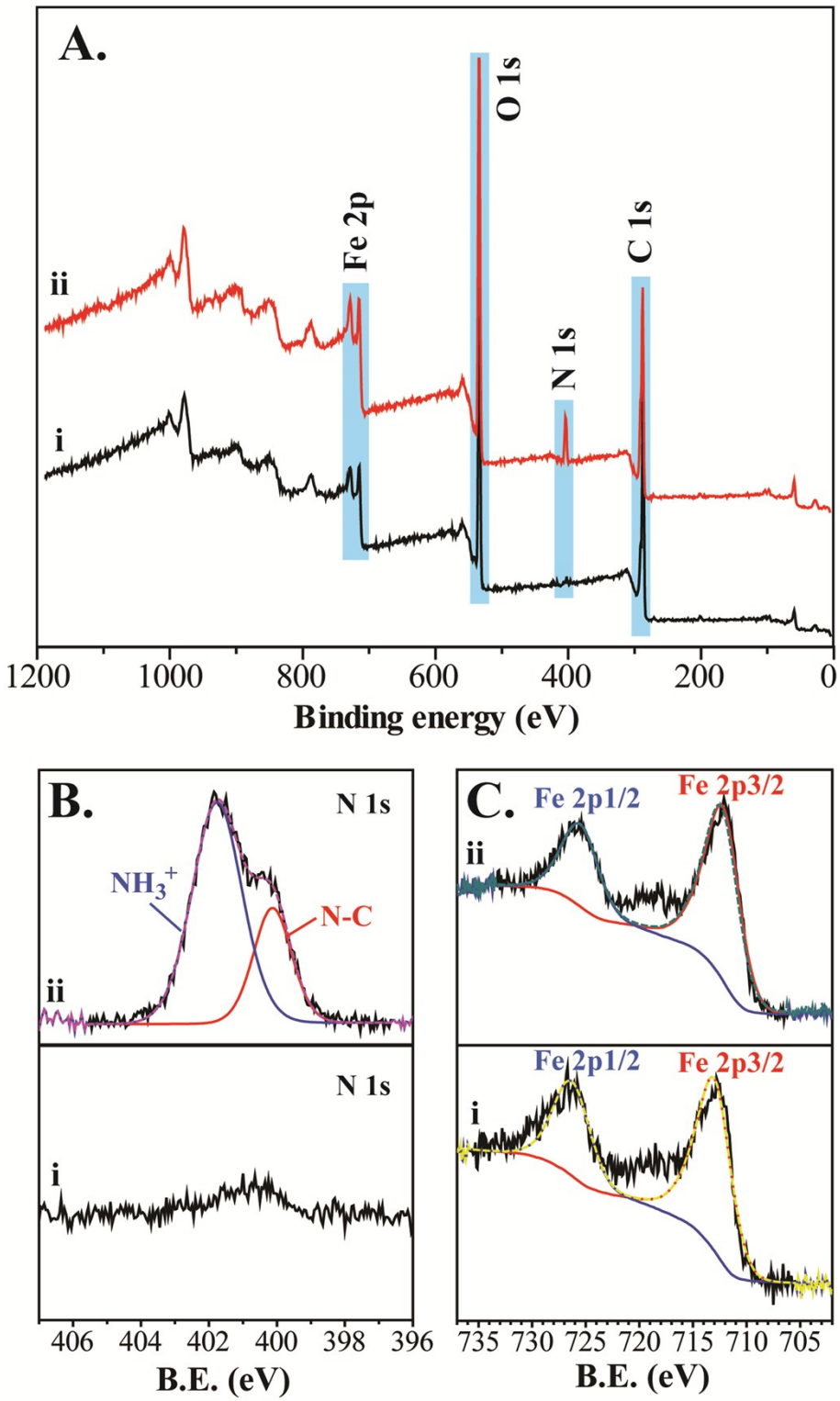

Figure S3. (A) X-ray photoelectron spectroscopy (XPS) spectra of (i) MIL-53(Fe) and (ii) glycine/MIL-53(Fe) composite. (B-C) N 1s and Fe 2p high resolution spectra of (i) MIL-53(Fe) and (ii) glycine/MIL-53(Fe) composite, respectively.

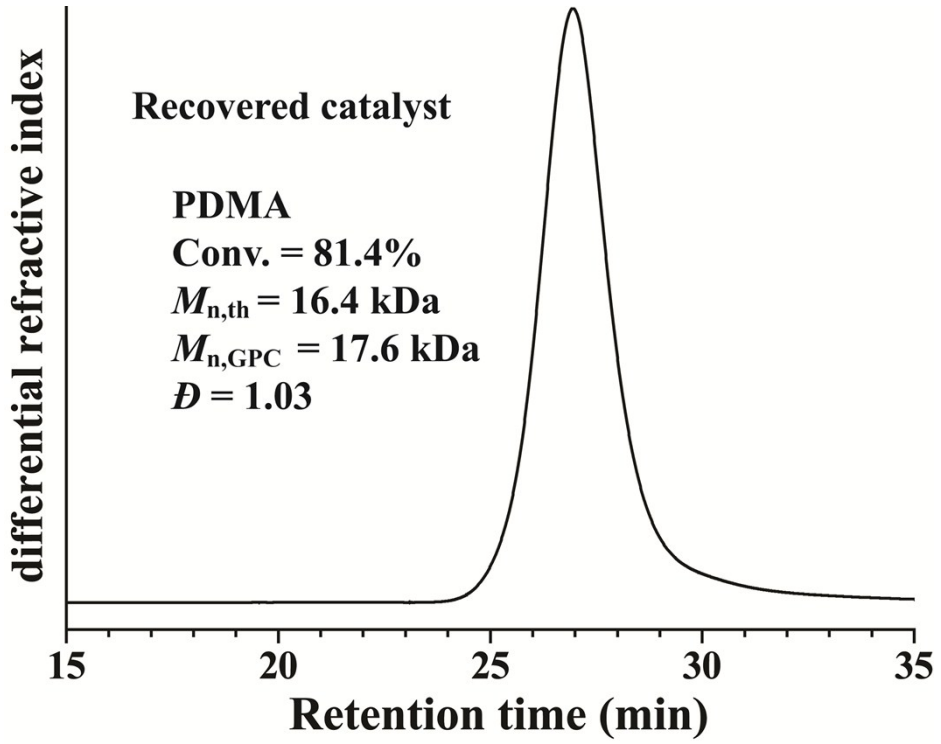

Figure S4. GPC profile of the prepared PDMA using recovered catalyst.

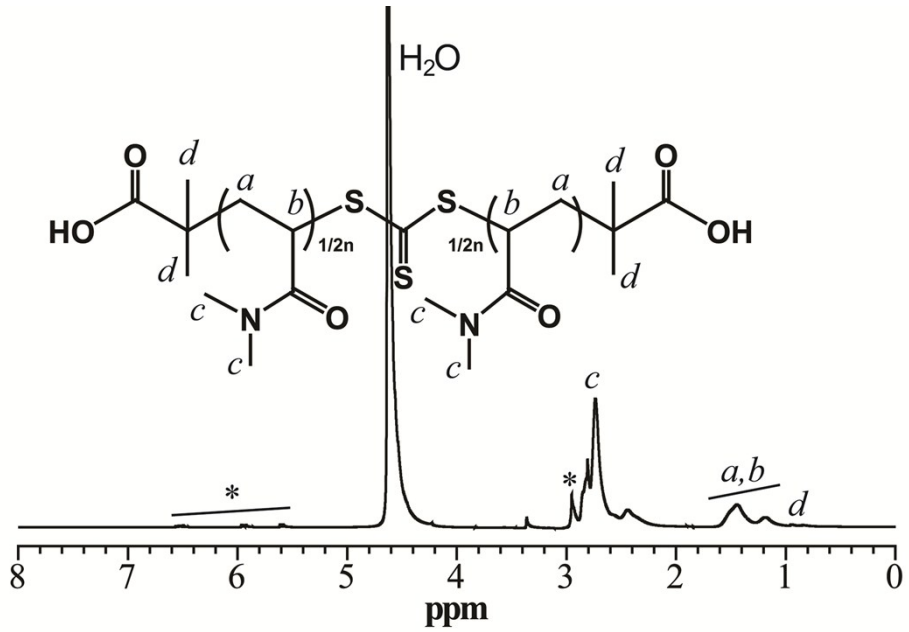

Figure S5. ^{1}H NMR spectrum of the synthesized PDMA (in D_2O). *These peaks are assigned to unreacted DMA monomer.

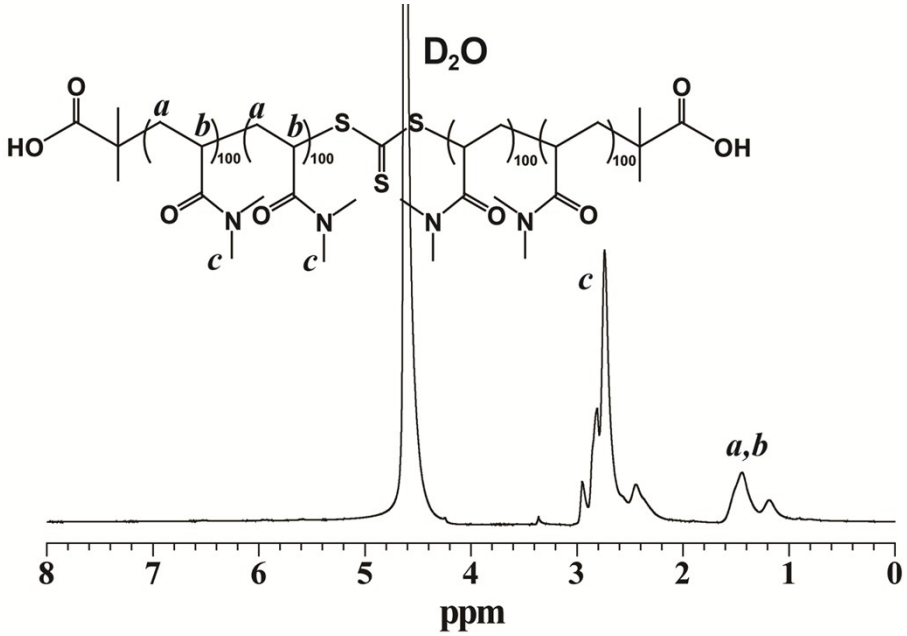

Figure S6. ^{1}H NMR spectrum of the synthesized *pseudo* block copolymer PDMA-*b*-PDMA-*b*-PDMA (in D_2O).

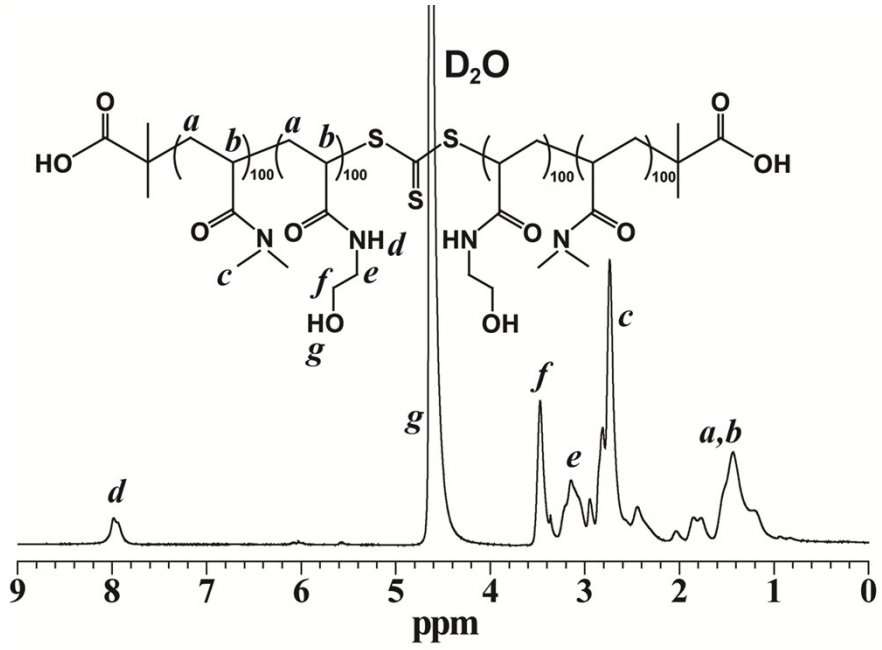

Figure S7. ^{1}H NMR spectrum of the synthesized block copolymer PDMA-*b*-PNHEA-*b*-PDMA (in D_2O).

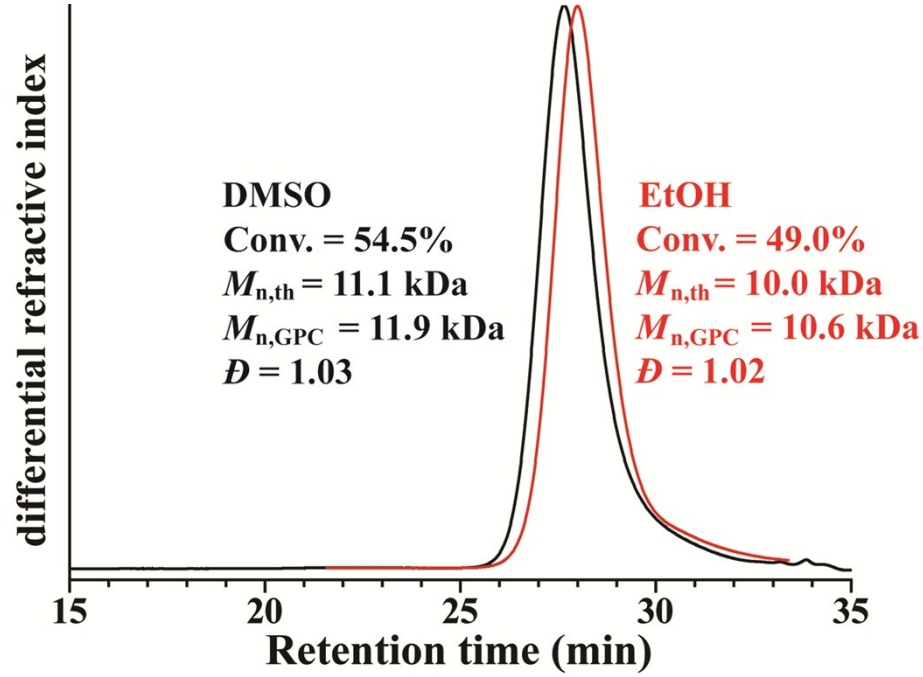

Figure S8. GPC profiles of the prepared PDMA polymers in DMSO (black trace) and EtOH (red trace) with targeted DP_n of 200.

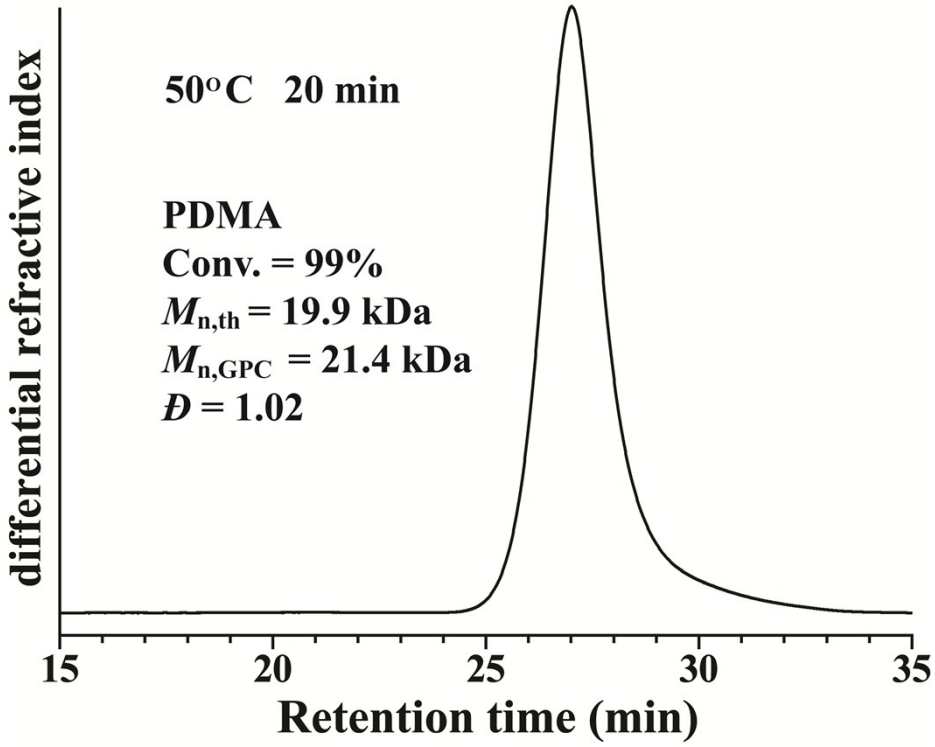

Figure S9. GPC profile of the prepared PDMA at 50 °C with a targeted DP_n of 200.

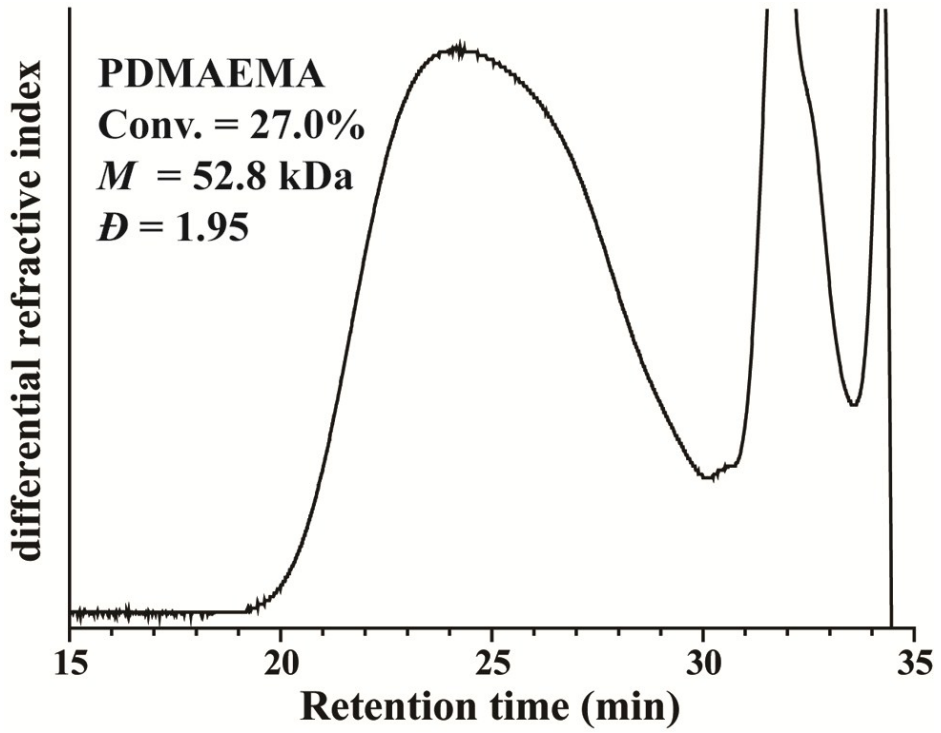

Figure S10. GPC profile of the prepared PDMAEMA in DI H_2O with a targeted DP_n of 200.

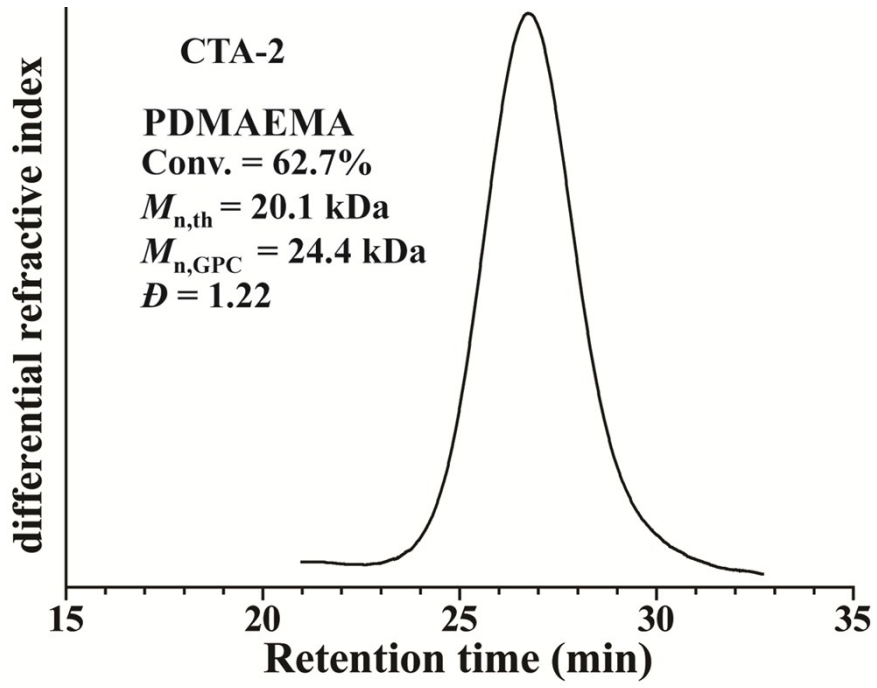

Figure S11. GPC profile of the prepared PDMAEMA using CTA-2 in DI H_2O with a targeted DP_n of 200.

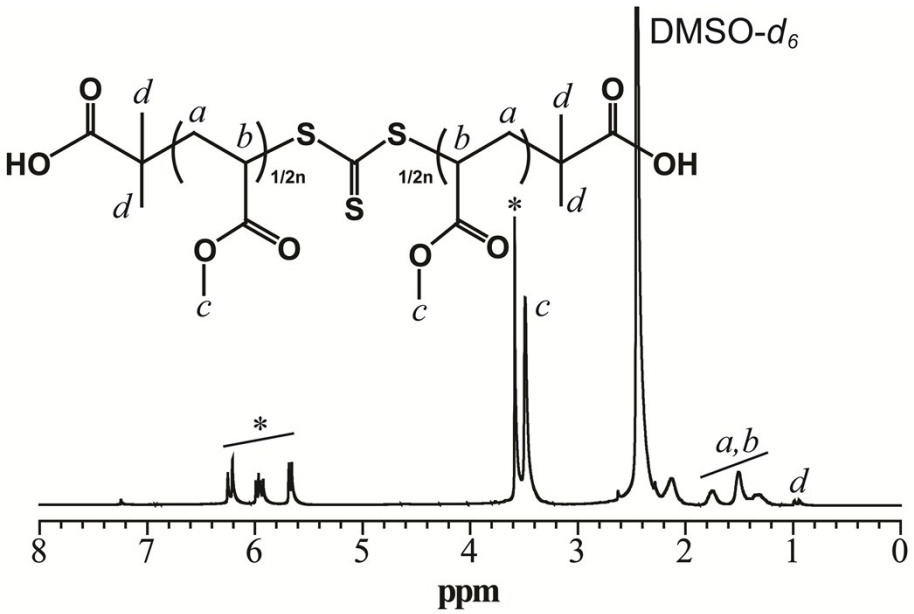

Figure S12. ^{1}H NMR spectrum of the synthesized PMA (in DMSO-d_6). *These peaks are assigned to unreacted MA monomer.

Table S1. Supplementary materials for Figure 4.

***	8121.4	8207.4	8292.5	(m/z)
HOOC, H	n=93.04	n=94.03	n=95.02	
HOOC, COOH	n=92.04	n=93.04	n=94.02	

***Theoretical number of repeat units of the RAFT polymer products.

As shown in Figure S13, the generation rate of H_2O_2 (0.43 M/h) is almost identical to the degradation rate (0.47 M/h) in the presented enzymatic cascade system.

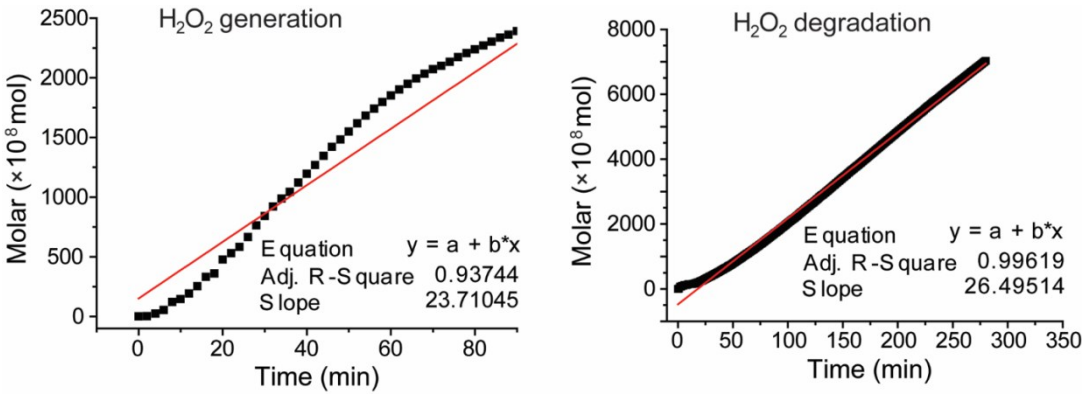

Figure S13. The investigation on the generation and degradation rates of H_2O_2 in the presented system.

References

1. Lai, J. T.; Filla, D.; Shea, R., Functional Polymers from Novel Carboxyl-Terminated Trithiocarbonates as Highly Efficient RAFT Agents. *Macromolecules* 2002, *35* (18), 6754-6756.
2. Ai, L.; Li, L.; Zhang, C.; Fu, J.; Jiang, J., MIL-53(Fe): A Metal–Organic Framework with Intrinsic Peroxidase-Like Catalytic Activity for Colorimetric Biosensing. *Chem. Eur. J.* 2013, *19* (45), 15105-15108.
3. Dong, W.; Yang, L.; Huang, Y., Glycine post-synthetic modification of MIL-53(Fe) metal–organic framework with enhanced and stable peroxidase-like activity for sensitive glucose biosensing. *Talanta* 2017, *167*, 359-366.