Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

One-step synthesis and regioselective polymerization of *N*α,*N*δ-bisphenoxycarbonyl-L-ornithine

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Experimental

Materials

Diphenyl carbonate (DPC, >99%) was purchased from TCI. Tetrabutylammonium hydroxide (TBAH, 40 wt% in MeOH), *N*,*N*-dimethylacetamide (DMAc, 99.8%, extra dry, with molecular sieves, water ≤50ppm), neopentylamine (98%) and L-ornithine (98%) were purchased from Energy Chemical (China) and used as received.

Measurements

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DMX 400 spectrometer (^{1}H: 400 MHz, ^{13}C: 100MHz) with DMSO-d_6 or D_2O as solvent, Chemical shifts (δ) were reported in ppm with tetramethylsilane (TMS) as internal reference. Matrix-assisted laser desorption ionization-time of flight (MALDI-ToF) mass spectra were collected on a Bruker UltraFLEX MALDI-ToF mass spectrometer. 2,5-Dihydroxybenzoic acid (DHB) was used as matric and potassium trifluoroacetate was used as the cationic agent. Molecular weights (MWs) and polydispersity indices ($Đ$) were determined by size exclusion chromatography (SEC), which consisted of a Wyatt series 1500 HPLC pump, a Wyatt Opitlab T-rEX interferometric refractometer (RI) and two MZ-Gel SDPlus columns of 10^2 Å 10 μm and 10^4 Å 10 μm. *N*,*N*-Dimethylformamide (DMF) containing 0.05 mol/L LiBr and 2‰ (v/v) triethylamine was used as eluent with a flow rate of 0.8 mL/min at 50 °C, and commercial polystyrenes were used as calibration standards. UV-vis transparency was recorded on a UV-2600 UV−vis spectrophotometer (Shimadzu) at a wavelength of 450 nm with a slit width of 2 nm. The polymer sample was dissolved in deionized water at room temperature and the T_{cp} were determined at $\lambda = 450$ nm and 50% transmittance.

Synthesis of N_α,N_δ-bis(phenoxycarbonyl)-L-ornithine (Orn(P)-NPC)

To a stirred suspension of L-ornithine (6.6 g, 50 mmol) in methanol (200 mL), a TBAH solution in methanol (32.4 g, 50 mmol) was added dropwise at room temperature. The solution was concentrated under reduced pressure to remove the methanol before acetonitrile (200 mL) was added to dissolve the mixture. The mixture was slowly added into an acetonitrile solution of DPC (21.4 g, 100 mmol) in 10 min. The solution was stirred at room temperature for 2 h, concentrated under reduced pressure, and dissolved by ethyl acetate. The mixture was acidified with 1 mol/L HCl until pH to 2-3 and extracted by ethyl acetate. The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography using petroleum ether/ethyl acetate as eluent. Recrystallization of the product in a mixture of ethyl acetate and petroleum ether yields 10.3 g Orn(P)-NPC (55%) as a white powder.

ESI-MS(*m/z*): calc. 373.13, found 373.11 ([Orn(P)-NPC]H^+); calc. 395.12, found 395.37 ([Orn(P)-NPC]Na^+); calc. 767.74, found 767.27 ($[\text{Orn(P)-NPC}]_2Na^+$); calc.743.75, found 743.11 ($[\text{Orn(P)-NPC}]_2$ -H^+). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.37 – 1.96 (4 H, m), 3.10 (2H, q), 4.03 (1H, m), 7.02 – 7.44 (10H, m), 7.79 (H, t), 8.13 (1H, d), 12.74 (1H, s). ^{13}C NMR (101 MHz, DMSO-d_6) δ 25.95, 28.10, 53.76, 121.60, 121.73, 124.83, 124.99, 129.19, 129.27, 150.94, 151.08, 154.33, 154.42, 173.48. IR (neat, cm^{-1}): 1716 (urethan (C=O)), 1595, 1530, 1490.

Polymerization of Orn(P)-NPC

As a typical example of polymerization in a flame-dried Schlenk flask, Orn(P)-NPC (372 mg, 1 mmol) was dissolved in DMAc (2.0 mL) followed by the addition of neopentylamine (1.45 mg, 0.017 mmol). Acidic acid (10.29 mg, 0.17 mmol) was added to suppress unwanted side reactions ($[\text{NPC}]_0$:$[\text{amine}]_0$:$[\text{acid}]_0$= 20:1:10). The polymerization was conducted at 60 °C under argon atmosphere for 24 h. The precipitate from diethyl ether was isolated by centrifugation and washed by diethyl ether twice. After the polymer is dried in vacuum, 179 mg of polyOrn(P) (76.4%) was obtained. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.81 (m), 1.47 (m), 3.04 (m), 4.04 (m), 7.01(m), 7.56 (m), 8.31 (m). ^{13}C NMR (101 MHz, DMSO-d_6) δ 25.59, 27.70, 67.48, 122.14, 125.24, 129.56, 151.45, 154.79. IR (neat, cm^{-1}): 1716 (urethan (C=O)), 1651 (amide (C=O)), 1545, 1490.

Synthesis of polyCit

PolyOrn(P) (50 mg, 0.2 mmol) was dissolved in THF (1 mL). Aqueous solution of 25 wt% $NH_3 \cdot H_2O$ (140 mg, 2 mmol) was added dropwise and the mixture was stirred at room temperature overnight. After dialysis against deionized water and lyophilization, 22 mg polyCit (70%) was obtained. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.77 (m), 1.26 (m), 2.90 (m), 3.98 (m), 5.74 (m), 7.92 (m). ^{13}C NMR (101 MHz, DMSO-d_6) δ 14.15, 27.16, 31.99, 65.50, 159.01, 175.18.

Synthesis of polyOrn

PolyOrn(P) (50 mg, 0.2 mmol) was dissolved in THF (1 mL). Aqueous solution (2 mL) of NaOH (80 mg, 2 mmol) was added dropwise. The mixture was stirred at room temperature overnight before dialysis against deionized water and lyophilization to yield 18 mg polyOrn (79%). ^{1}H NMR (400 MHz, deuterium oxide) δ 0.76 (d), 1.68 (m), 2.94 (m), 4.25 (m). ^{13}C NMR (101 MHz, deuterium oxide) δ 23.28, 26.44, 28.05, 38.87, 53.09, 173.30.

Synthesis of polyArg

PolyOrn(P) (100 mg, 0.4 mmol) was dissolved in THF (2 mL). Aqueous solution (4 mL) of NaOH (160 mg, 4 mmol) was added dropwise. The mixture was stirred at room temperature overnight and then evaporated to remove THF. Aqueous solution (2 mL) of o-methylisourea hemisulfate (0.98g, 4mmol) was added and the pH of mixture was adjusted to 12 by NaOH aqueous solution. The guanidination procedure is conducted at 65 °C for 10 min without further separation of the produced polyOrn. The mixture was then dialyzed against deionized water and lyophilized to yield 53 mg polyArg (85%). ^{1}H NMR (400 MHz, deuterium oxide) δ 0.81 (m), 1.70 (d), 3.17 (m), 4.27 (m). ^{13}C NMR (101 MHz, deuterium oxide) δ 24.50, 26.42, 28.07, 40.51, 53.41, 156.65, 173.56.

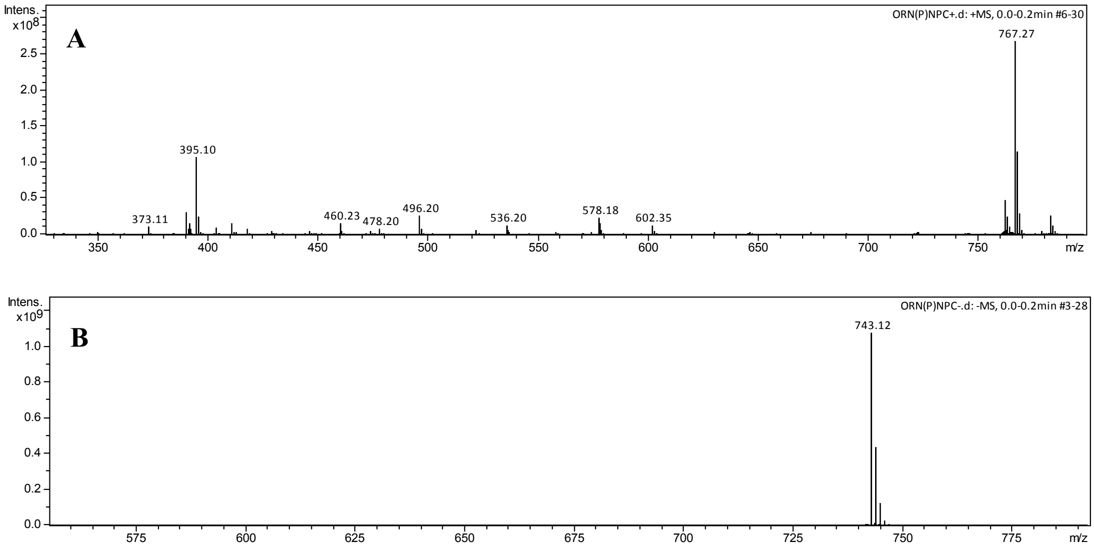


Figure S1. Mass spectra of Orn(P)-NPC, calc. 373.13, found 373.11 [Orn(P)-NPC]H$^+$); calc. 395.12, found 395.37 ([Orn(P)-NPC]Na$^+$); calc. 767.74, found 767.27 ([Orn(P)-NPC]$_2$Na$^+$); calc.743.75, found 743.11 ([Orn(P)-NPC]$_2$ -H$^+$).

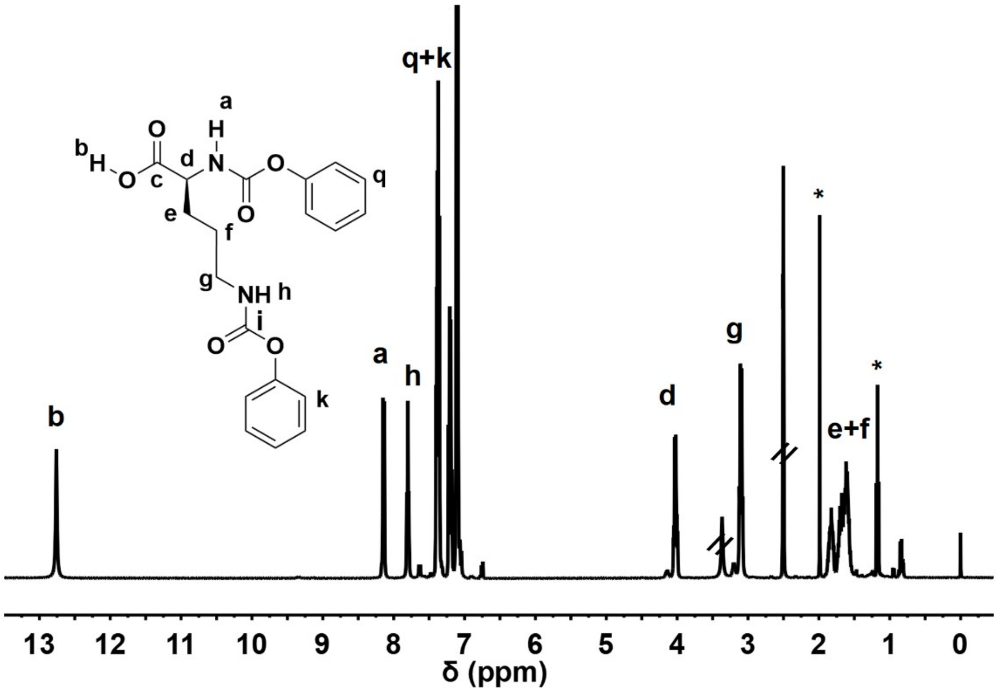


Figure S2. ^{1}H NMR of Orn(P)-NPC in DMSO-d_6.

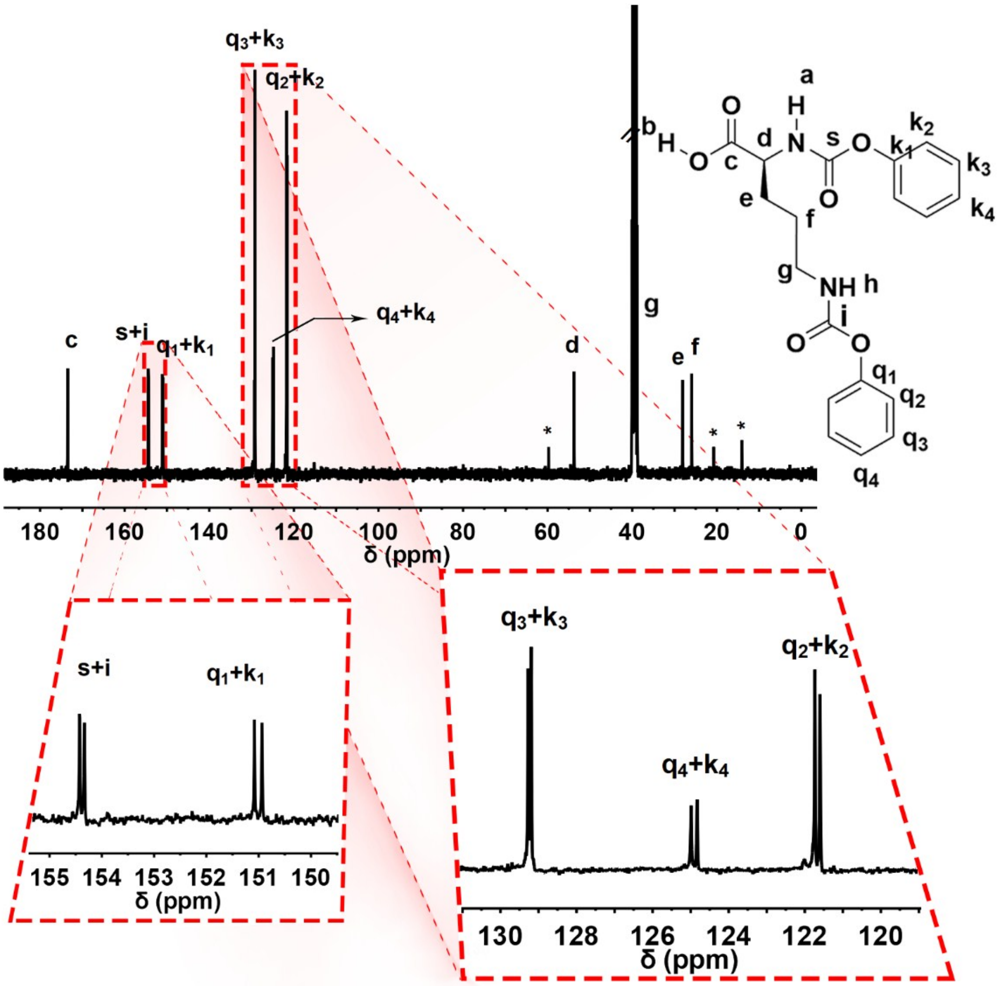


Figure S3. ^{13}C NMR of Orn(P)-NPC in DMSO-d_6 (*: ethyl acetate).

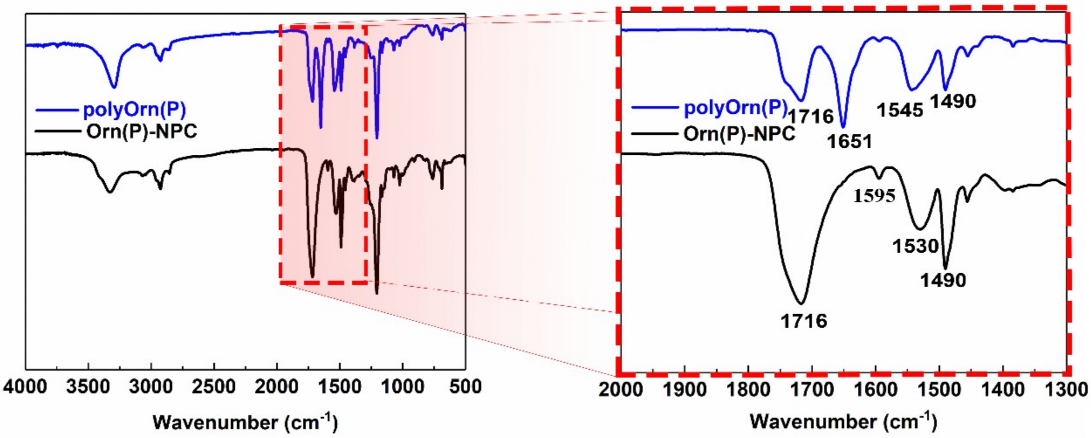


Figure S4. Infrared spectra of Orn(P)-NPC and polyOrn(P).

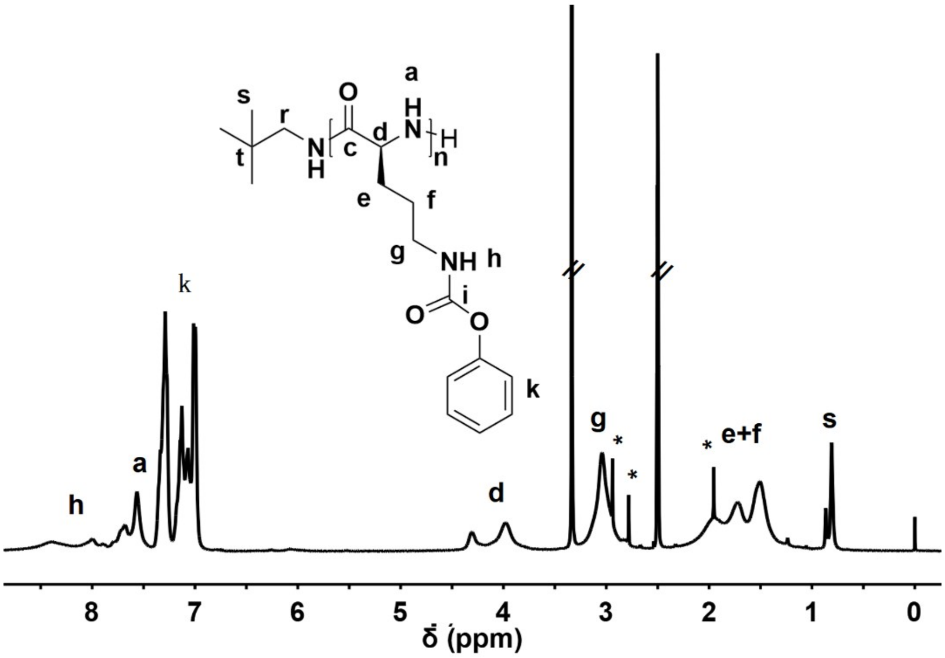


Figure S5. ^{1}H NMR of polyOrn(P) ($[NPC]_0$:$[amine]_0$= 20:1) in DMSO-d_6 (*: DMAc).

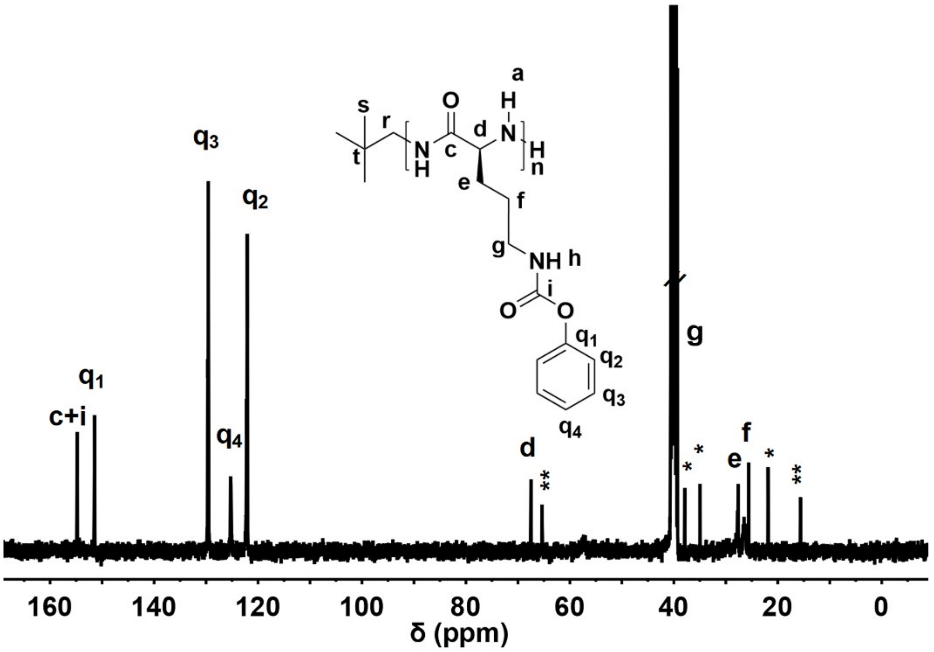


Figure S6. ^{13}C NMR of polyOrn(P) ($[NPC]_0$:$[amine]_0$= 20:1) in DMSO-d_6 (*: DMAc, **: diethyl ether).

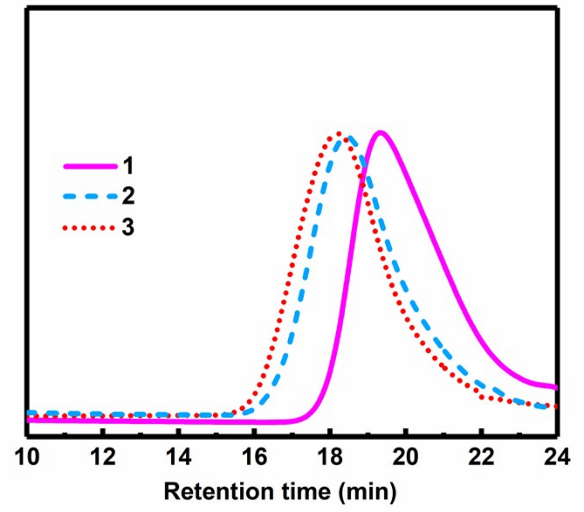


Figure S7. SEC traces of polyOrn(P) of samples 1, 2 and 3 in Table 1.

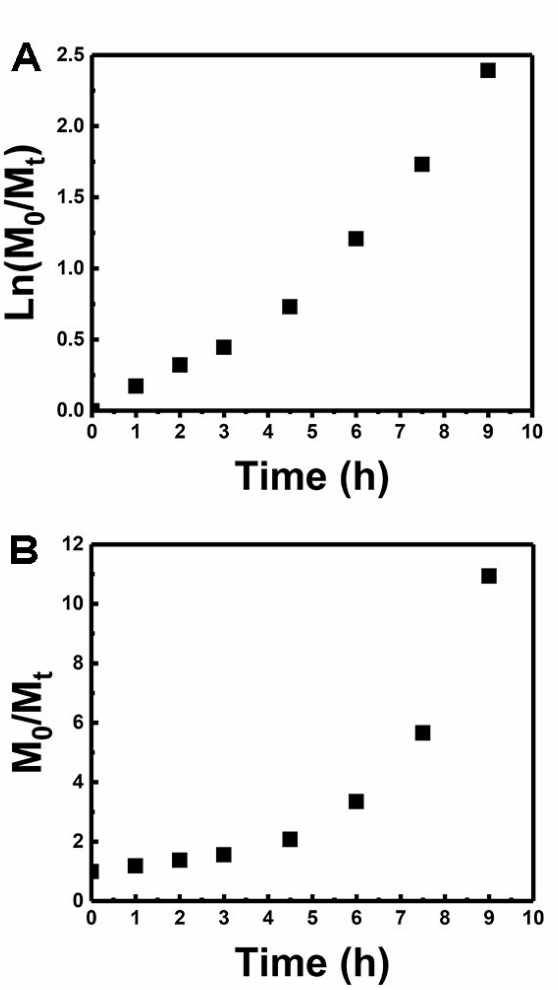


Figure S8. Polymerization kinetics of Orn(P)-NPC with first- (A) and second-order fittings (B).

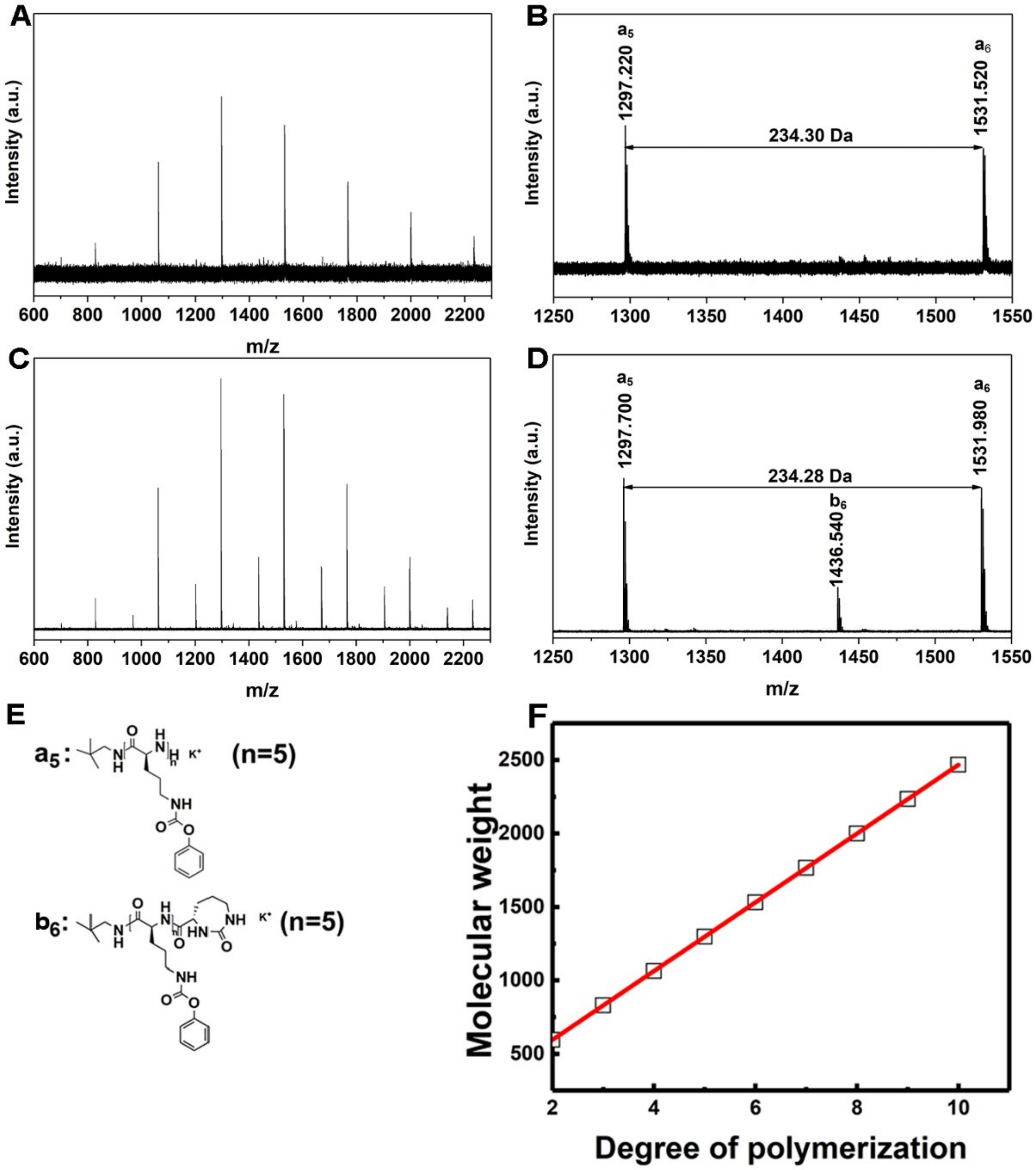


Figure S9. MALDI-ToF mass spectra of polyOrn(P) with 10 equivalents of AcOH to amine at conversions of 60% (A) and 80% (C) with their zoom-in views (B and D), the corresponding chemical structures (E) and plot of molecular weight vs. degree of polymerization (F) of population a (black squares) and its fitting line (red line), slope: 234.08 (R^2= 0.99).

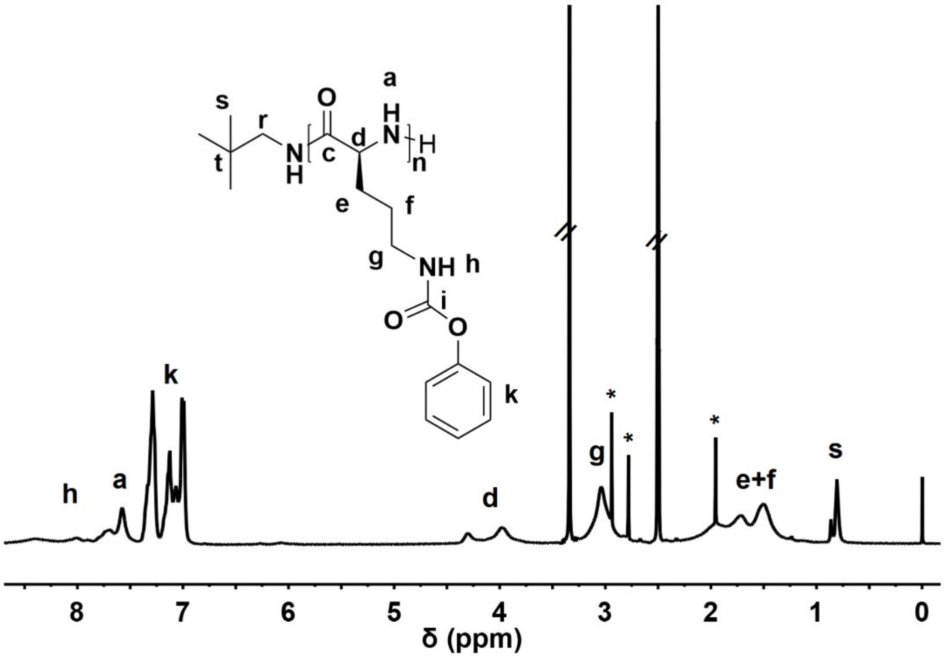


Figure S10. ^{1}H NMR of polyOrn(P) without acetic acid ($[NPC]_0$:$[amine]_0$= 20:1, DP_{NMR}=18) in DMSO-d_6 (*: DMAc).

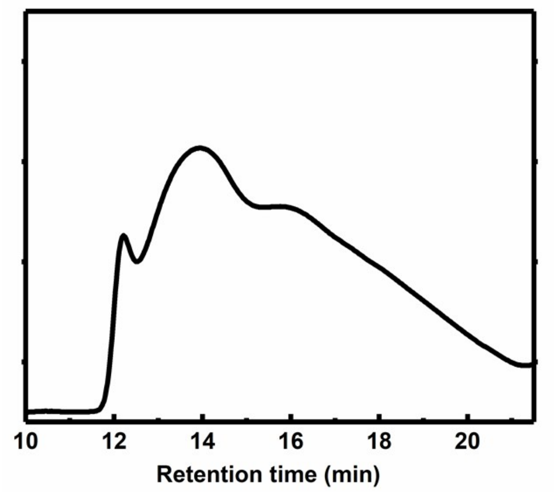


Figure S11. SEC trace of polyOrn(P) without acetic acid ($[NPC]_0$:$[amine]_0$:$[acid]_0$= 20:1:0).

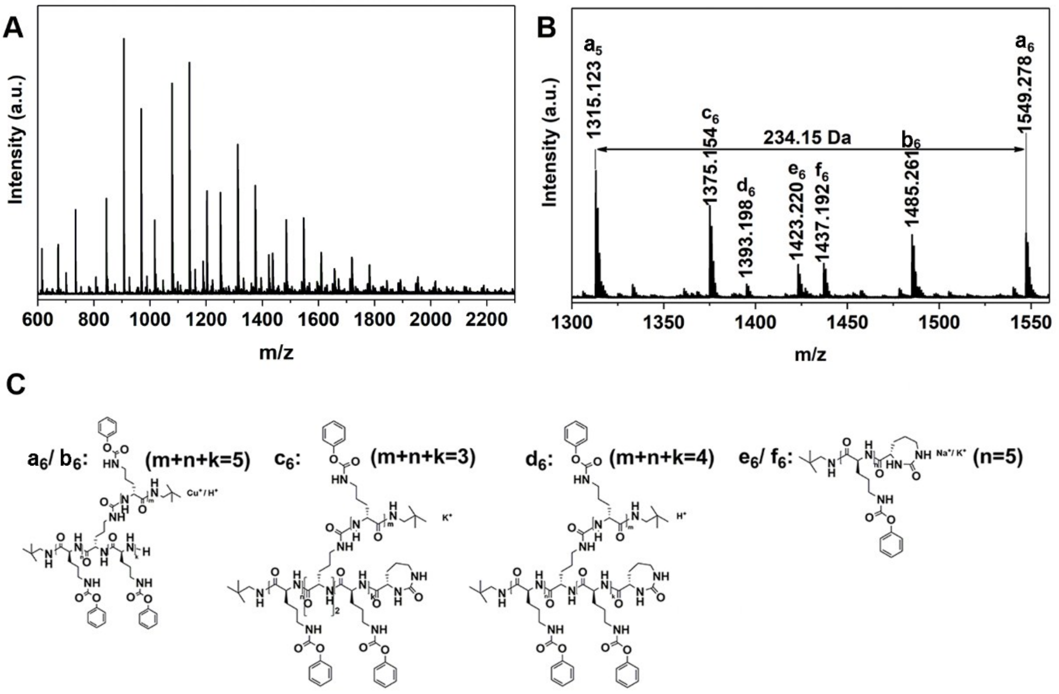
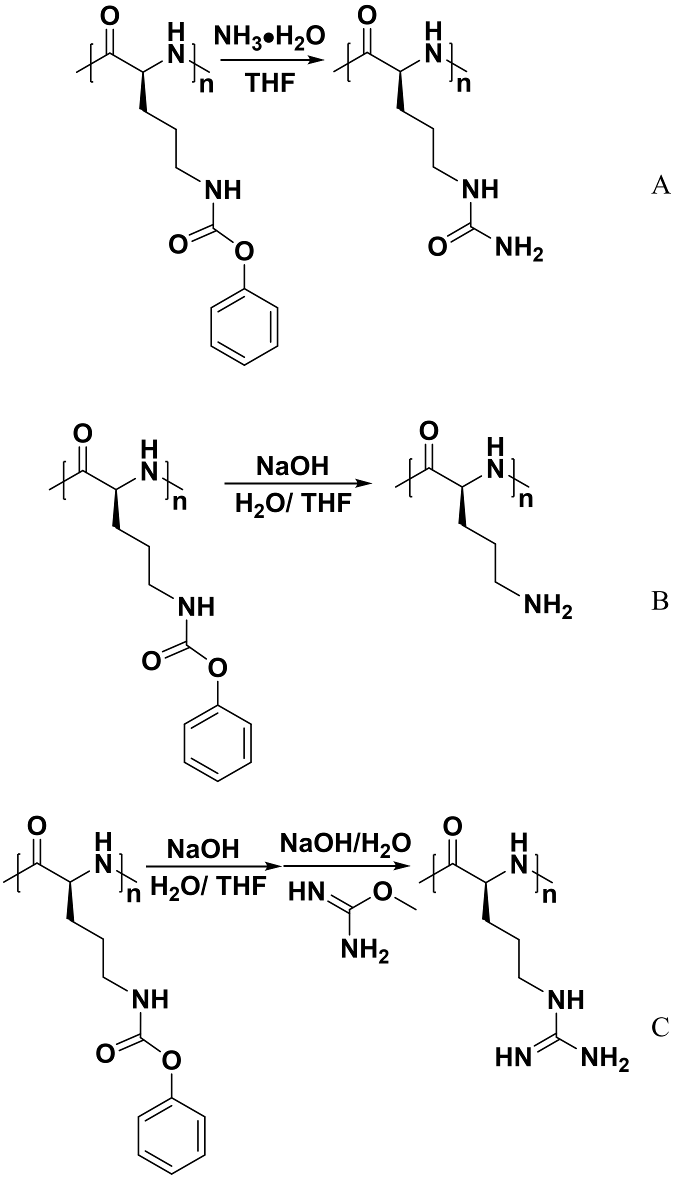


Figure S12. MALDI-ToF mass spectrum of polyOrn(P) without acetic acid (A) with its zoom-in views (B), and the corresponding chemical structures (C).



Scheme S1. Syntheses of polyCit (A), polyOrn (B) and polyArg (C).

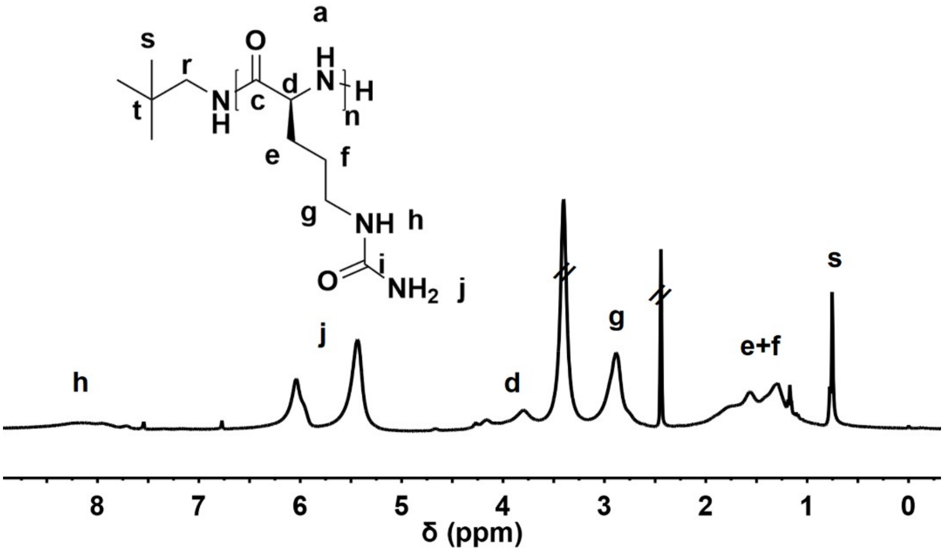


Figure S13. ^{1}H NMR of polyCit in DMSO-d_6.

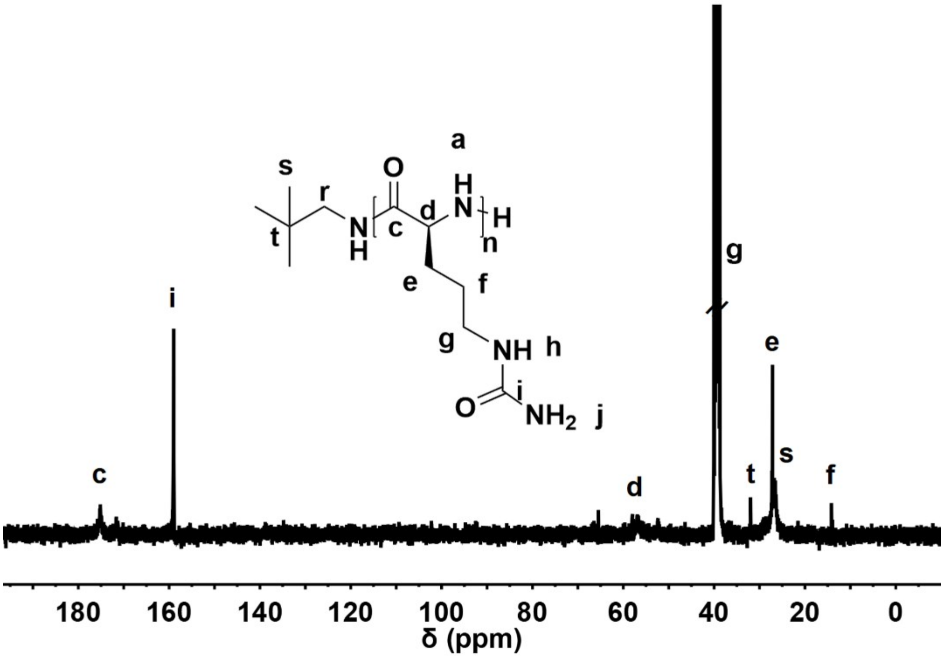


Figure S14. ^{13}C NMR of polyCit in DMSO-d_6.

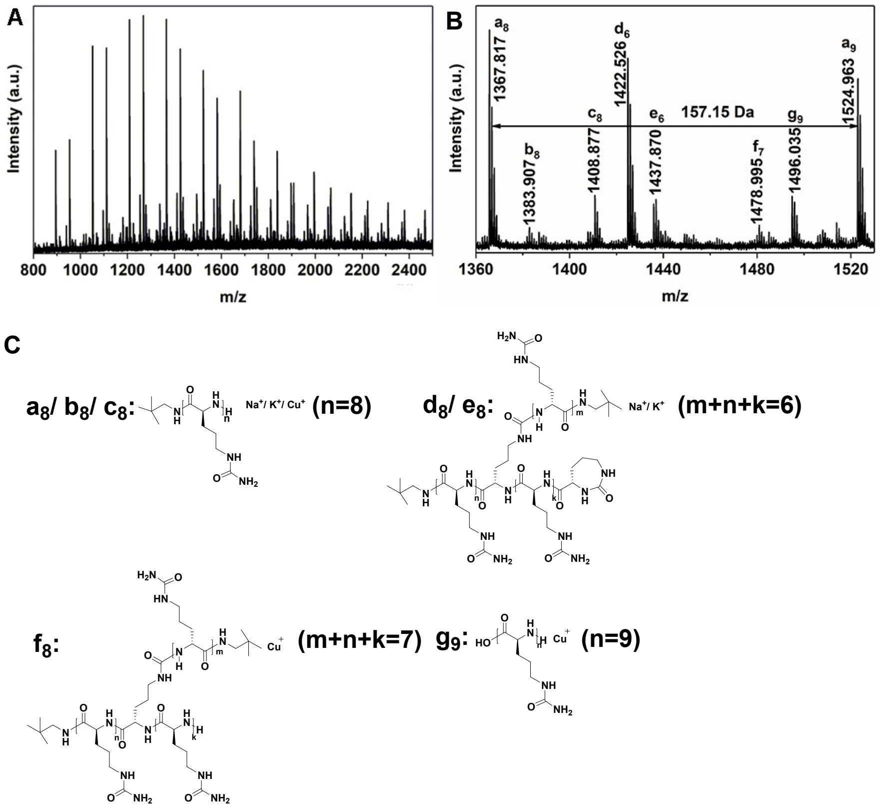


Figure S15. MALDI-ToF mass spectrum of polyCit (A) with its zoom-in view (B) and the corresponding chemical structures (C).

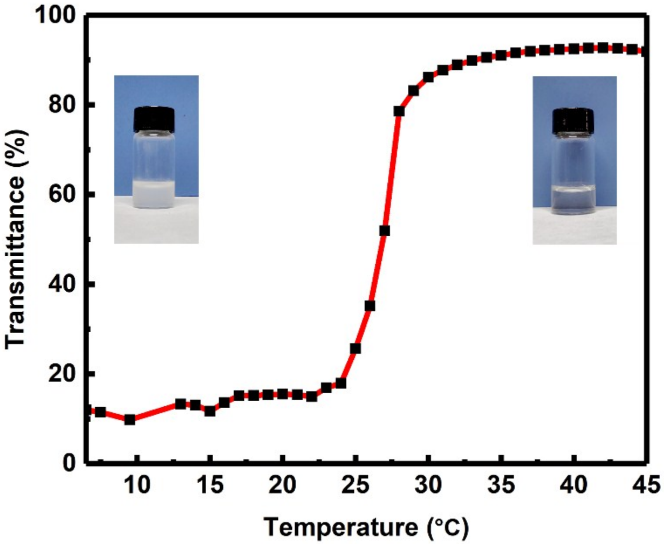


Figure S16. Transmittance changes at λ = 450 nm as a function of temperature for the aqueous solution of polyCit (DP=60) with a concentration of 2.0 mg/mL (Inset: photographs of polyCit aqueous solution at 10 (left) and 35 °C (right)).

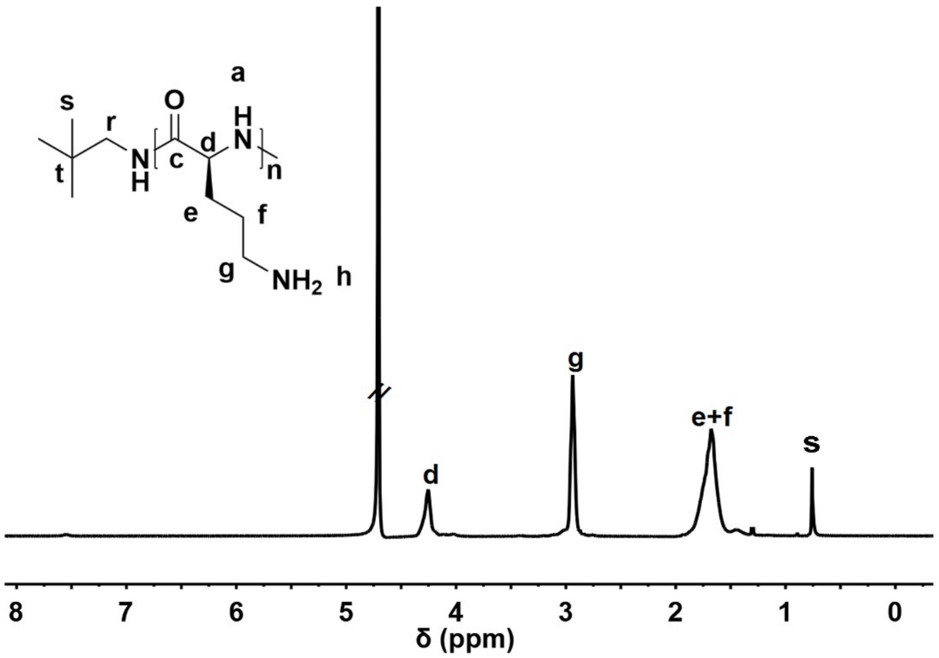


Figure S17. ^{1}H NMR of polyOrn in D_2O.

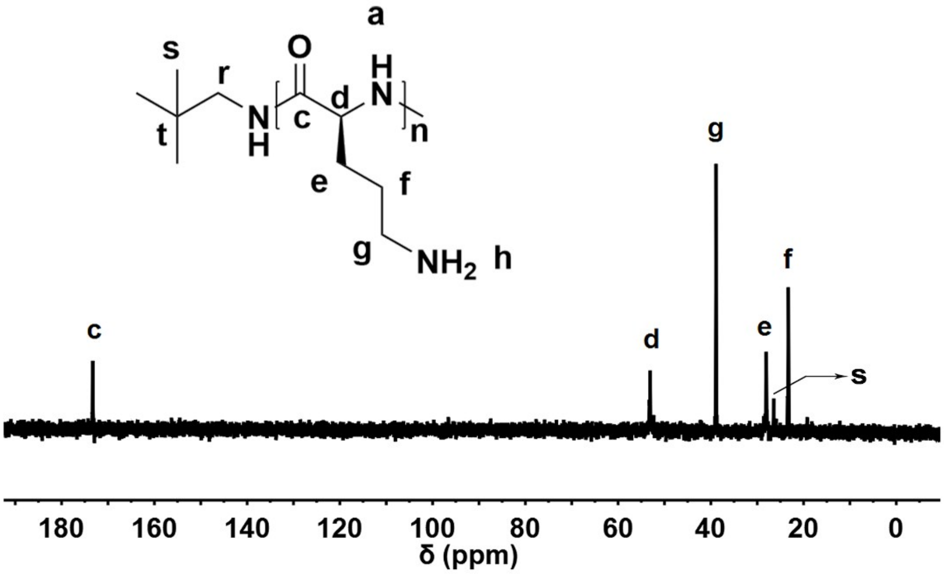


Figure S18. ^{13}C NMR of polyOrn in D_2O.

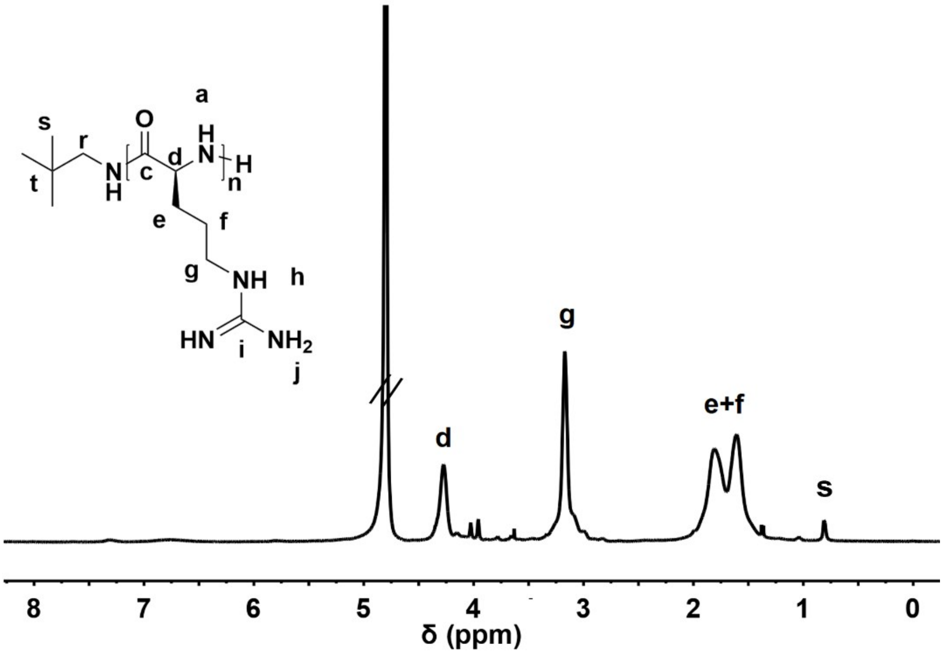


Figure S19. ^{1}H NMR of polyArg in D_2O.

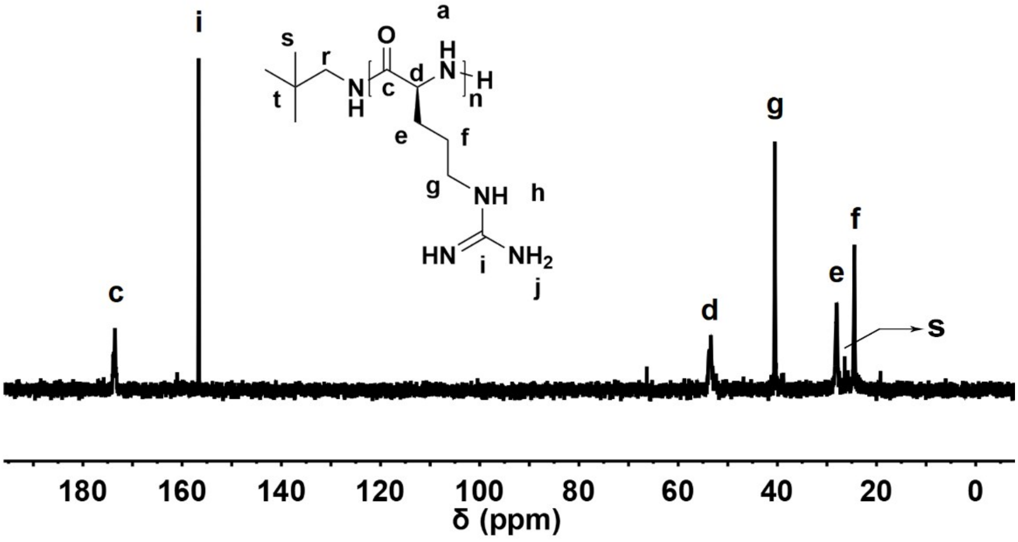


Figure S20. ^{13}C NMR of polyArg in D_2O.