Electronic Supplementary Information

Nitrocatecholic Copolymers – Synthesis and

their Remarkable Binding Affinity

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1. General Information

N-isopropylacrylamide (NIPAM, 98%, TCI) was purified by recrystallization in hexanes/toluene (v:v=70/30) and dried under a vacuum. 2, 2-Azobisisobutyronitrile (AIBN, 98%, Sigma-Aldrich) was purified by recrystallization in methanol. Chloroform (99%, Sigma-Aldrich) was washed with water to remove ethanol and distilled over anhydrous Na_2SO_4. *N, N*-Dimethylformamide (DMF, 99%, Acros) was distilled over CaH_2. Dopamine hydrochloride (99%, Alfa Aesar), methacrylic anhydride (97%, Sigma-Aldrich), sodium tetraborate decahydrate (99%, Alfa Aesar), sodium bicarbonate (99.7%, Sigma-Aldrich), ferrous chloride hexahydrate (99.5%, Fisher), sodium sulfite (98%, Sigma-Aldrich), tetrabutylammonium fluoride (TBAF, 1.0 M in THF, Sigma-Aldrich), *tert*-butyldimethylsilyl chloride (TBDMS-Cl, 97%, Sigma-Aldrich), nitric acid (reagent ACS, Acros), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 98%, Sigma-Aldrich), acetic anhydride (99.5%, Sigma-Aldrich), phosphotungstic acid (PTA, reagent grade, Sigma-Aldrich), catechol (99%, Alfa Aesar), 4-nitrocatechol (99%, Alfa Aesar) and 4-fluorophenylboronic acid (FPBA, Sigma-Aldrich) were used as received.

All NMR spectra were conducted in deuterated dimethyl sulfoxide (DMSO-d6), deuterated chloroform (CD_3Cl) or 10 % of D_2O in PBS solution, respectively, with an Agilent VNMRS-600 MHz spectrometer using a 5mm HCN cryoprobe. The data were processed using SpinWorks or VNMRJ software.

^1H NMR spectra were collected using a single pulse sequence or presaturated water suppression pulse sequence with an observed frequency of 599.9414 MHz, 2.0 s relaxation delay, 2.0 µs pulse width and 64-512 scans.

^{13}C NMR spectra were performed at a resonance frequency of 150.87 MHz with a $\pi/4$ pulse width of 6.55 µs, 3.0 s recycle delay and 4000 scans.

2D ^1H-^{13}C heteronuclear multiple-bond correlation spectroscopy (HMBC) spectrum was carried out with J_{nCH} of 10 Hz and 1.5 s delay for long-range ^1H-^{13}C coupling selection. The number of transients was 248. Complex points were 1024 in ^1H direction. In ^{13}C dimension, the number of time increments was 128.

2D nuclear overhauser spectroscopy (NOESY) spectra of poly(6-nitrodopamine methacrylamide-*co*-*N*-isopropylacrylamide)-10% (P(*N*DMA-*co*-NIPAM))-10% and poly(6-nitrodopamine methacrylamide) (P*N*DMA) were recorded with the mixing time of 600 ms at 40 °C. The number of collected complex points was 1024 in the F2 dimension, and the recycle delay was 1.0 s. In the F1 dimension, 128 time increments were recorded.

FT-IR spectra were collected by a Bruker Vertex 70V FT-IR spectrometer equipped with a liquid nitrogen-cooled mercury-cadmium-telluride (MCT) detector or a deuterated triglycine sulphate (DTGS) detector at room temperature. The instrument was mounted with an attenuated total reflectance (ATR) accessary (Pike technologies, 20175) operating at 1 cm^{-1} resolution and 128-256 scans.

The molecular weights and molecular weight distribution, $\overline{M_w}/\overline{M_n}$ of copolymer samples were determined by a size exclusion chromatography system (Tosoh, HLC-8320GPC EcoSEC) equipped with refractive index using linear polystyrene standards which were applied for calibration at 40 ºC. THF was applied as eluent with a flow rate of 0.35 mL/min at 40 ºC. TEM images were taken on a FEI Tecnai Spirit microscope operated at an accelerating voltage of 120 kV. Before the imaging, the samples were sonicated in methanol and then drop-casted on carbon coated copper grids on filter paper, and the solvent was allowed to evaporate under air. For a stained sample, one drop of aqueous PTA (0.5 % by mass) was deposited on the copper grid with dried Fe_3O_4 nanoparticles (NPs). Wide-angle X-ray scattering (WAXS) pattern measurement was performed on a Bruker Nanostar U instrument equipped with a rotating anode Cu K_α X-ray source (operated at 50kV and 24mA) and with a 2-dimensional detector Vantec 2000. Thermogravimetric analysis (TGA) was carried out using a TA Instruments Q500 from 30 ºC-800 ºC at 5 ºC/min in air. The sonication was carried out using an Astrason Ultrasonic cleaner (Model 14, 60 KHz, 200 W) in ice-water for 30 minutes.

2. Syntheses of Polymers

2.1 Synthesis of dopamine methacrylamide (DMA)

Monomer DMA was synthesized based on modifications of a reported method.[1] Sodium tetraborate decahydrate (20.00 g) and sodium bicarbonate (8.00 g) were added to 200 mL of water. After bubbling the mixture with N_2 for 30 min, 10.00 g of dopamine hydrochloride (52.8 mmol) was added under N_2 protection. After stirring for another 2 hours, 9.4 mL of methacrylic anhydride (62.8 mmol) in 50 mL of tetrahydrofuran (THF) was then added dropwise into the reaction mixture. The reaction mixture was stirred for 14 h at room temperature under N_2 protection. Subsequently, the undissolved solid was filtered out and the pH of filtrate was adjusted to lower than 2. The acidified aqueous solution was kept in refrigerator to precipitate out crude product. The crude product (5.51 g) was purified by recrystallization from methanol/water (v:v=9:1). The purified product was dried under a vacuum at 60 ºC (3.05 g, 26 %).

^{1}H NMR (600 MHz, DMSO-d6) δ (ppm): 8.73 (s, 1H, C_6H_3(OH)(OH)-), 8.61 (s, 1H, C_6H_3(OH)(OH)-), 7.91 (t, 1H, C_6H_3(OH)$_2$-CH_2-CH_2-NH-C(=O)-), 6.60 (d, 1H, C_6H_2H(OH)$_2$-), 6.55 (s, 1H, C_6H_2H(OH)$_2$-), 6.40 (d, 1H, C_6H_2H(OH)$_2$-), 5.59 (s, 1H, -C(=O)-C(CH$_3$)=CHH), 5.27 (s, 1H, -C(=O)-C(CH$_3$)=CHH), 3.21 (q, J=7.0 Hz, 2H, -CH$_2$-CH_2-NH-C(=O)-), 2.53 (t, J=7.7 Hz, 2H, C_6H_3(OH)$_2$-CH_2-CH$_2$-), 1.82(s, 3H, -C(=O)-C(CH_3)=CH$_2$).

^{13}C NMR (600 MHz, DMSO-d6) δ (ppm): 167.26 (1C, -NH-C(=O)-C(CH$_3$)=CH$_2$), 140.06 (1C, -NH-C(=O)-C(CH$_3$)=CH$_2$), 145.02-115.39 (6C, C_6H$_3$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 118.79 (1C, -NH-C(=O)-

C(CH$_3$)=CH$_2$), 40.94 (1C, C$_6$H$_3$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 34.58 (1C, C$_6$H$_3$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 18.67 (1C, -C(=O)-C(CH$_3$)=CH$_2$). Italics indicate the atom generating the peak.

2.2 Protection of DMA with TBDMS-Cl (Synthesis of *N*-(3, 4-bis((*tert*-butyldimethylsilyl)oxy) phenethyl)methacrylamide (*S*DMA))

TBDMS-Cl (6.80 g, 45.1 mmol) and 3.26 g of DMA (14.7 mmol) were dissolved in 40 mL of DMF. The solution was cooled in a dry ice bath for 10 min, followed by addition of DBU (7 mL, 46.8 mmol). After the reaction was stirred in a dry ice bath for 4 h and an additional 20 h at room temperature, the solid was removed by filtration.

The filtrate was diluted with 250 mL of water and the crude product was extracted with 600 mL of hexane three times. The hexane was removed with a rotary evaporator after it was dried over anhydrous Na$_2$SO$_4$. The crude product was purified with hexane:ethyl acetate (v:v=90:10) using silica column chromatography to give 2.05 g of white solid (31 %).

^{1}H NMR (600 MHz, CDCl$_3$) δ (ppm): 6.75 (d, 1H, C$_6$H$_2$$H$(OTBDMS)$_2$-), 6.66 (s, 1H, C$_6H_2$$H$(OTBDMS)$_2$-), 6.62 (d, 1H, C$_6H_2$$H$(OTBDMS)$_2$-), 5.77 (t, 1H, -CH$_2$-CH$_2$-N$H$-C(=O)-), 5.58 (s, 1H, -C(=O)-C(CH$_3$)=CHH), 5.26 (s, 1H, -C(=O)-C(CH$_3$)=CHH), 3.49 (q, J=6.4 Hz, 2H, -CH$_2$-CH_2-NH-C(=O)-), 2.71 (t, J=7.2 Hz, 2H, C$_6$H$_3$(OTBDMS)$_2$-CH_2-CH$_2$-), 1.89 (s, 3H, -C(=O)-C(CH_3)=CH$_2$), 0.97 (s, 18H, -Si(CH$_3$)$_2$-C(CH_3)$_3$), 0.17 (s, 12H, -Si(CH_3)$_2$-C(CH$_3$)$_3$).

^{13}C NMR (600 MHz, CDCl$_3$) δ (ppm): 168.48 (1C, -NH-C(=O)-C(CH$_3$)=CH$_2$), 140.29 (1C, -NH-C(=O)-C(CH$_3$)=CH$_2$), 146.96-121.29 (6C, C_6H$_3$(OTBDMS)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 119.47 (1C, -NH-C(=O)-C(CH$_3$)=CH$_2$), 40.75 (1C, C$_6$H$_3$(OTBDMS)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 34.83 (1C, C$_6$H$_3$(OTBDMS)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 18.8 (1C, -C(=O)-C(CH$_3$)=CH$_2$), 18.64 (6C, -Si(CH$_3$)$_2$-C(CH$_3$)$_3$), -3.90 (4C, -Si(CH$_3$)$_2$-C(CH$_3$)$_3$). Italics indicate the atom generating the peak.

2.3 Preparation of Poly(*O*,*O*'-bis(*tert*-butyldimethylsilyl)dopamine metharylamide-*co*-*N*-isopropylacrylamide) (P(*S*DMA-*co*-NIPAM))

In a typical polymerization, 1.26 g of *S*DMA (2.8 mmol), 2.92 g of NIPAM (25.8 mmol) and 24 mg of AIBN (0.15 mmol) were dissolved in 14 mL of DMF. Polymerization was conducted at 80 ºC for 24 h after the solution bubbled with N$_2$ for 30 min. The polymer was precipitated out with 20 mL of water and

purified by washing with boiling hexane in a Soxhlet extractor for 24 h. About 4.0 g of copolymer was obtained after drying in a vacuum at room temperature.

^{1}H NMR (600 MHz, CDCl$_3$) δ (ppm): 7.14 (m, 1H, br, -NH-C(=O)-), 6.75 (s, 1H, C$_6$H$_2$$H$(OTBDMS)$_2$-CH$_2$-), 6.62-6.57 (d, 2H, C$_6$$H$$_2$H(OTBDMS)$_2$-CH$_2$-), 3.91 (s, 1H, -C$H$(CH$_3$)$_2$), 3.29 (s, br, 2H, -C$H_2$-NH-C(=O)-), 2.60 (s, br, 2H, -CH_2-C$_6$H$_3$(OTBDMS)$_2$), 2.24 (m, br, 1H, -CH(C=O)-CH$_2$-), 1.80-1.63 (m, br, 2H, -CH(C=O)-CH_2- and m, br, 2H, -C(C=O)(CH$_3$)-CH_2-), 1.11 (s, 6H, (CH_3)$_2$CH- and s, 3H, -C(C=O)(CH_3)-CH$_2$-), 0.96 (s, 18H, -Si(CH$_3$)$_2$-C(CH_3)$_3$), 0.17 (s, 12H, -Si(CH_3)$_2$-C(CH$_3$)$_3$). Italics indicate the atom generating the peak.

2.4 Preparation of poly(dopamine methacrylamide-*co*-*N*-isopropylacrylamide) (P(DMA-*co*-NIPAM))

The preparation of P(DMA-*co*-NIPAM) by deprotection of P(*S*DMA-*co*-NIPAM) is similar to the deprotection in the synthesis of P(*N*DMA-*co*-NIPAM) in 2.5. The NMR peak assignment is based on references.[2]

^{1}H NMR (600 MHz, DMSO-d6) δ (ppm):8.62 (s, br, 2H, C$_6$H$_3$(OH)$_2$-), 7.18 (m, 1H, br, -NH-C(=O)-), 6.62-6.55 (d, 2H, C$_6$HH_2(OH)$_2$-), 6.40 (s, 1H, C$_6$$HH_2(OH)_2$-), 3.83 (s, 1H, -C$H$(CH$_3$)$_2$), 3.08 (s, br, 2H, -C$H_2$-NH-C(=O)-), 2.59 (s, br, 2H, -CH_2-C$_6$H$_3$(OH)$_2$), 1.94 (m, br, 1H, -C(C=O)H-CH$_2$-), 1.44 (m, br, 2H, -C(C=O)H-CH_2- and m, br, 2H, -C(C=O)(CH$_3$)-CH_2-, backbone of NIPAM and DMA), 1.03 (s, 6H, (CH_3)$_2$CH- and s, 3H -C(C=O)(CH_3)-CH$_2$-).

^{13}C NMR (600 MHz, DMSO-d6) δ (ppm): 173.35 (1C, -NH-C(=O)-), 144.98-115.50 (6C, C_6H$_3$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 45.29 (1C, -C(CH$_3$)(C=O)-CH$_2$-), 41.67-39.0 (1C, C$_6$H$_3$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-; 1C, -CH(CH$_3$)$_2$ and 1C, -CH$_2$-CH(C=O)-), 39.0-34.58 (1C, C$_6$H$_3$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-; 1C, -CH$_2$-CH(C=O)- and -C(CH$_3$)(C=O)-CH$_2$-), 22.19 (1C, -C(C=O)(CH$_3$)-CH$_2$- and 2C, -CH(CH$_3$)$_2$). Italics indicate the atom generating the peak.

2.5 Preparation of P(*N*DMA-*co*-NIPAM)

After 0.45 g of P(*S*DMA-*co*-NIPAM) was dissolved in 5 mL of CHCl$_3$ in an ice bath, cool concentrated nitric acid (0.16 mL) in acetic anhydride (1.6 mL) was added dropwise into the polymer solution. The

solution was stirred in the ice bath for 20 min with reaction progress monitored using ^{1}H NMR. After complete nitration, 0.5 g of ascorbic acid was added. The mixture was stirred for 2 h using 20 mL of hexane for precipitation. The precipitate was washed using boiling hexane in a Soxhlet apparatus for 24 h. After drying thoroughly in a vacuum, the precipitate was dissolved in 5 mL of THF/methanol (4.5:0.5) and treated with 1 mL of TBAF/THF (1 M). After stirring for 2 h, the polymer precipitate was collected and washed using boiling hexane in a Soxhlet apparatus for 24 h. The polymer was further purified by six times reprecipitating using 5 mL of methanol and 10 mL of HCl (pH=2) before drying in a vacuum, with a final yield of 0.25 g of polymer.

^{1}H NMR (600 MHz, DMSO-d6) δ (ppm): 10.38 (s, 1H, (NO$_2$)C$_6$H$_2$(OH)(OH)-), 9.78 (s, 1H, (NO$_2$)C$_6$H$_2$(OH)(OH)-), 7.44 (s, 1H, (NO$_2$)C$_6$$H$H(OH)$_2$-), 7.16 (m, 1H, br, -N$H$-C(=O)-), 6.70 (s, 1H, (NO$_2$)C$_6$HH(OH)$_2$-), 3.81 (s, 1H, -CH(CH$_3$)$_2$), 3.17 (s, br, 2H, -CH_2-NH-C(=O)-), 2.86 (s, br, 2H, -CH_2-C$_6$H$_2$(NO$_2$)(OH)$_2$), 1.93 (m, br, 1H, -C(C=O)H-CH$_2$-), 1.42 (m, br, 2H, -C(C=O)H-CH_2- and m, br, 2H, -C(C=O)(CH$_3$)-CH_2-, backbone of NIPAM and *N*DMA), 1.02 (s, 6H, (CH_3)$_2$CH- and s, 3H, -C(C=O)(CH_3)-CH$_2$-).

^{13}C NMR (600 MHz, DMSO-d6) δ (ppm): 173.79 (1C, -NH-C(=O)-), 151.66-112.57 (6C, (NO$_2$)C_6H$_2$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 45.3 (1C, -C(CH$_3$)(C=O)-CH$_2$-), 42.0-39.0 (1C, (NO$_2$)C$_6$H$_2$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-; 1C, -CH(CH$_3$)$_2$ and 1C, -CH$_2$-CH(C=O)-), 39.0-34.6 (s, 1C, -C(CH$_3$)(C=O)-CH$_2$- and 1C, -CH$_2$-CH(C=O)-), 33.2 (1C, (NO$_2$)C$_6$H$_2$(OH)$_2$-CH$_2$-CH$_2$-NH-C(=O)-), 22.71 (1C, -C(C=O)(CH$_3$)-CH$_2$- and 2C, -CH(CH$_3$)$_2$). Italics indicate the atom generating the peak.

2.6 Preparation of P*N*DMA

The procedure is similar to the synthesis of P(*N*DMA-*co*-NIPAM) in 2.5.

^{1}H NMR (600 MHz, DMSO-d6) δ (ppm): 10.32 (s, 1H, (NO$_2$)C$_6$H$_2$(OH)(OH)-), 9.67 (s, 1H, (NO$_2$)C$_6$H$_2$(OH)(OH)-), 7.39 (s, 1H, (NO$_2$)C$_6$HH(OH)$_2$- and 1H, br, -NH-C(=O)-), 6.69 (s, 1H, (NO$_2$)C$_6$HH(OH)$_2$-), 3.16 (s, br, 2H, -CH_2-NH-C(=O)-), 2.84 (s, br, 2H, -CH_2-C$_6$H$_2$(NO$_2$)(OH)$_2$), 1.67 (m, br, 2H, -C(C=O)(CH$_3$)-CH_2-), 0.86 (s, 3H, -C(C=O)(CH_3)-CH$_2$-). Italics indicate the atom generating the peak.
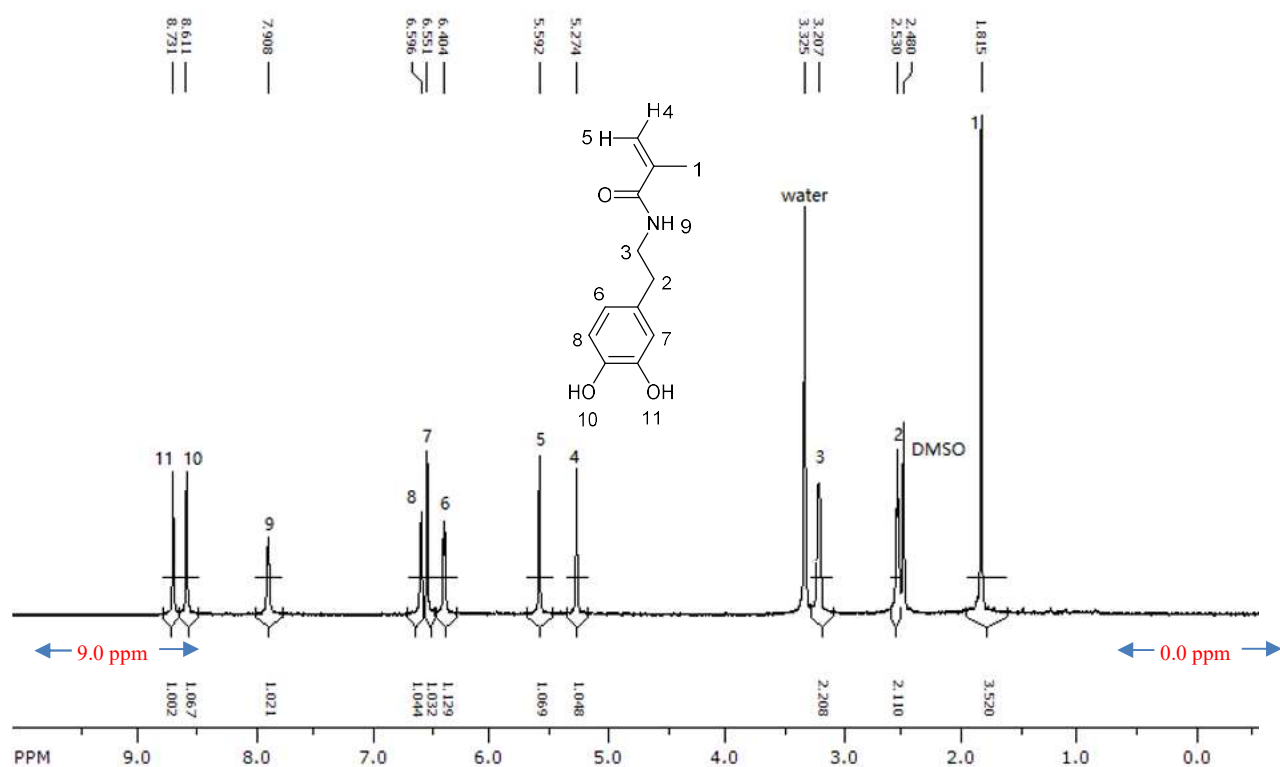
Fig. S1 ^{1}H NMR spectrum of DMA in DMSO-d6 at 25 °C.
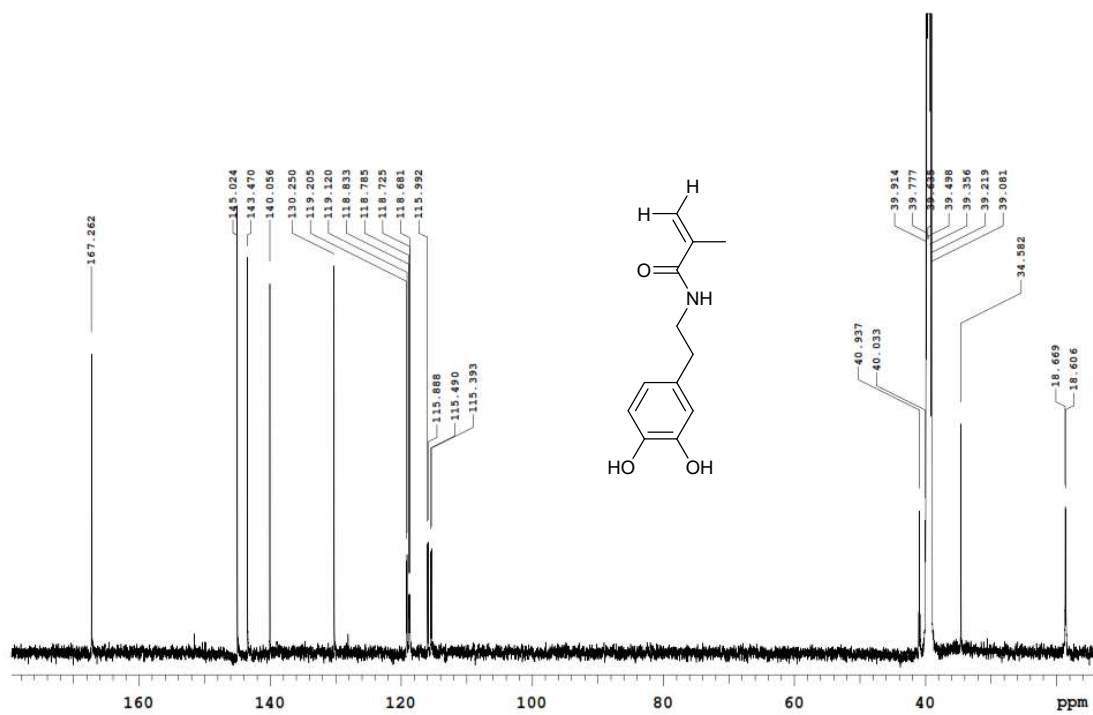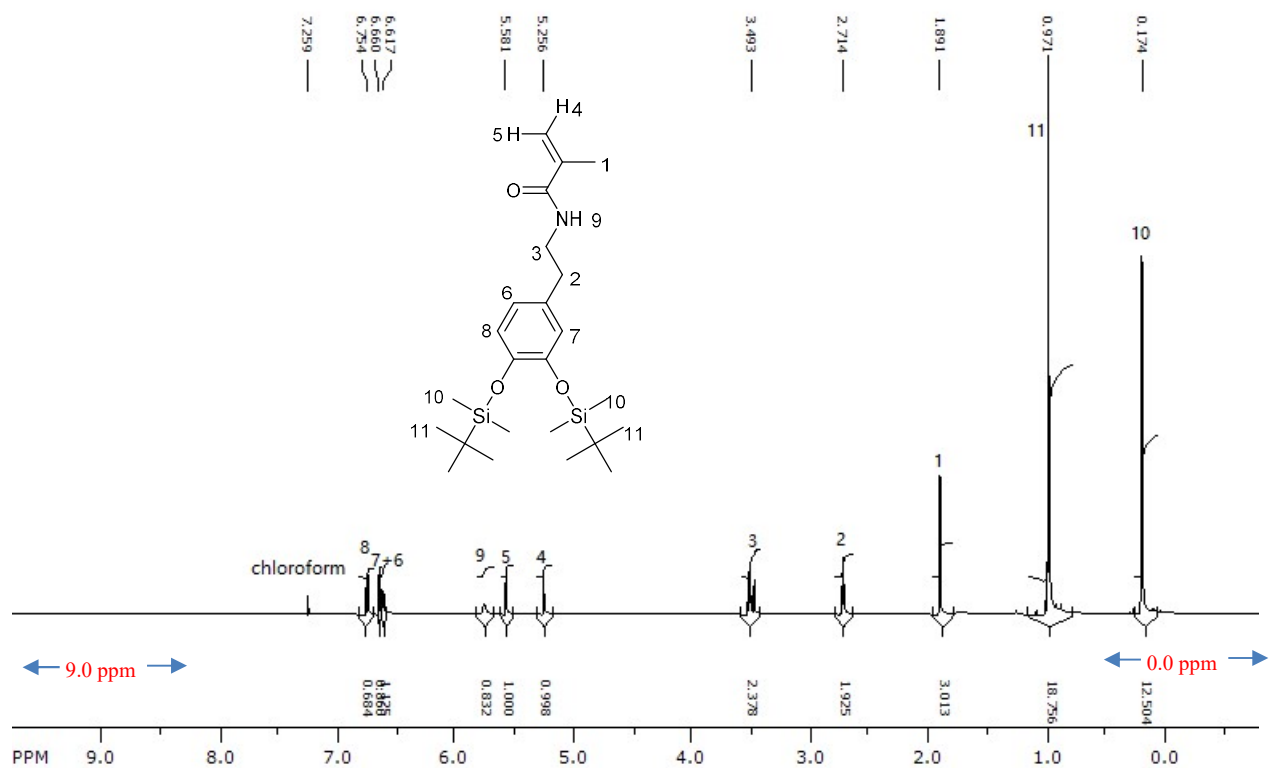

Fig. S2 ^{13}C NMR spectrum of DMA in DMSO-d6 at 25 °C.

Fig. S3 ^{1}H NMR spectrum of **S**DMA in chloroform-d at 25 °C.
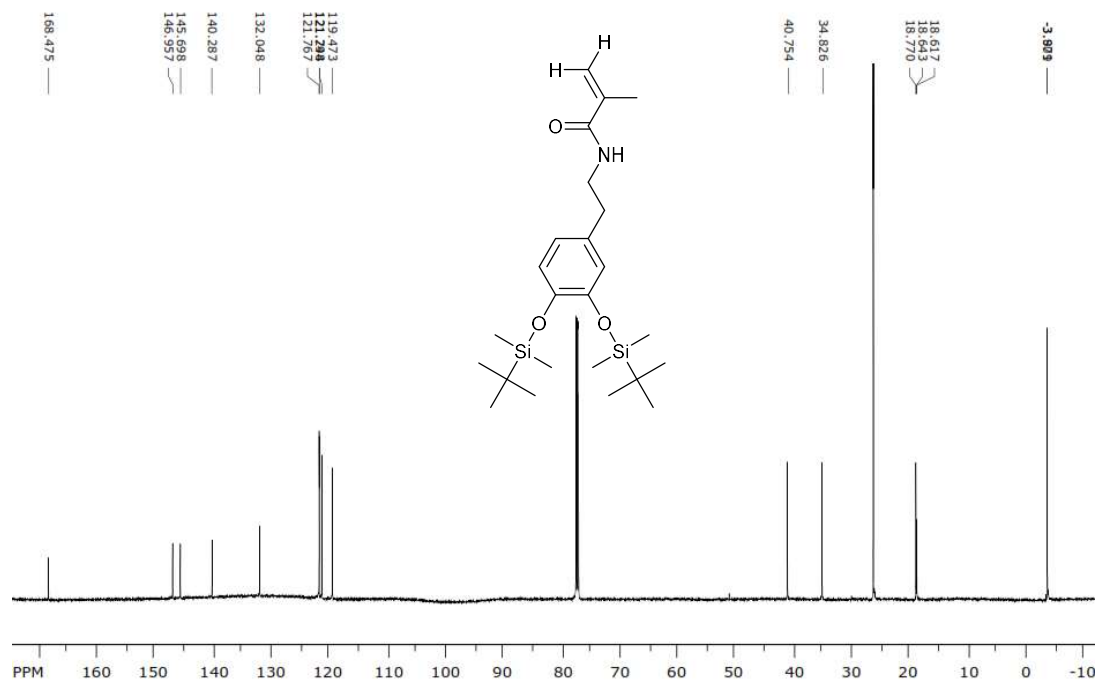

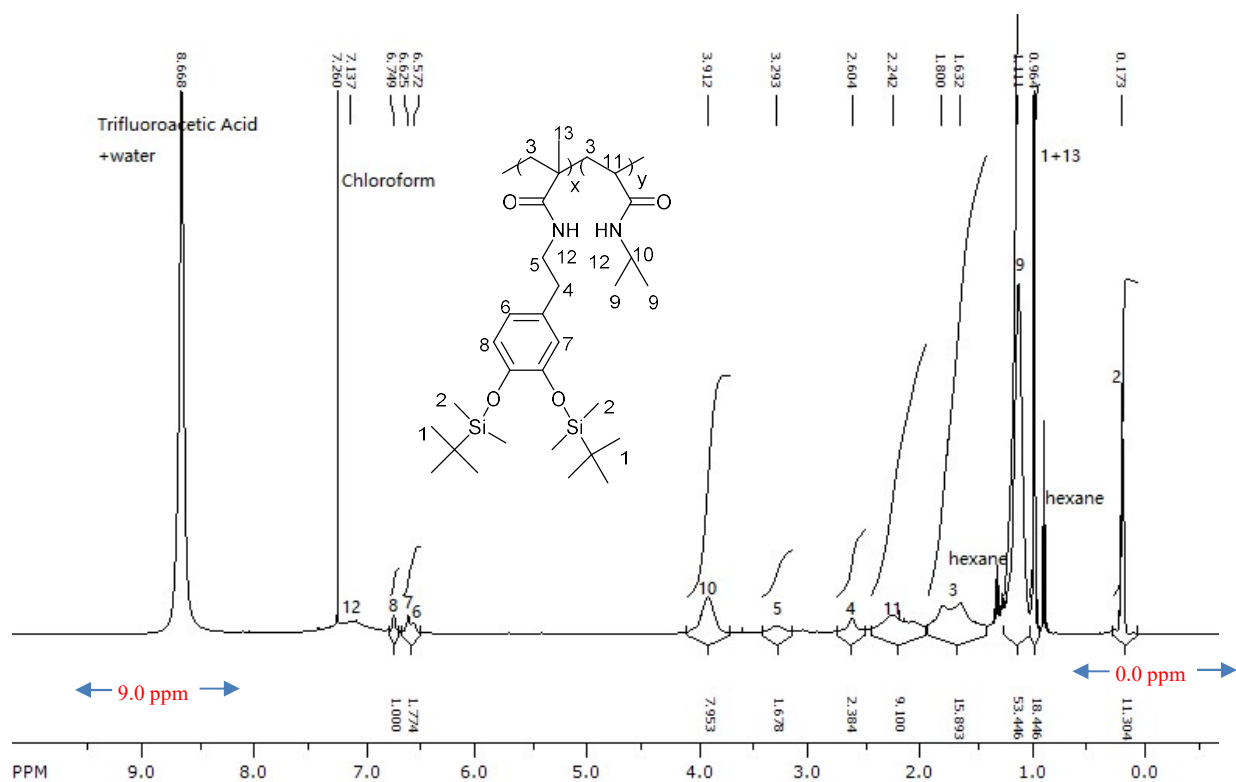**Fig. S4** ^{13}C NMR spectrum of **S**DMA in chloroform-d at 25 °C.

Fig. S5 ^{1}H NMR spectrum of P(**S**DMA-*co*-NIPAM) in chloroform-d (containing 4% trifluoroacetic acid) at 25 °C.
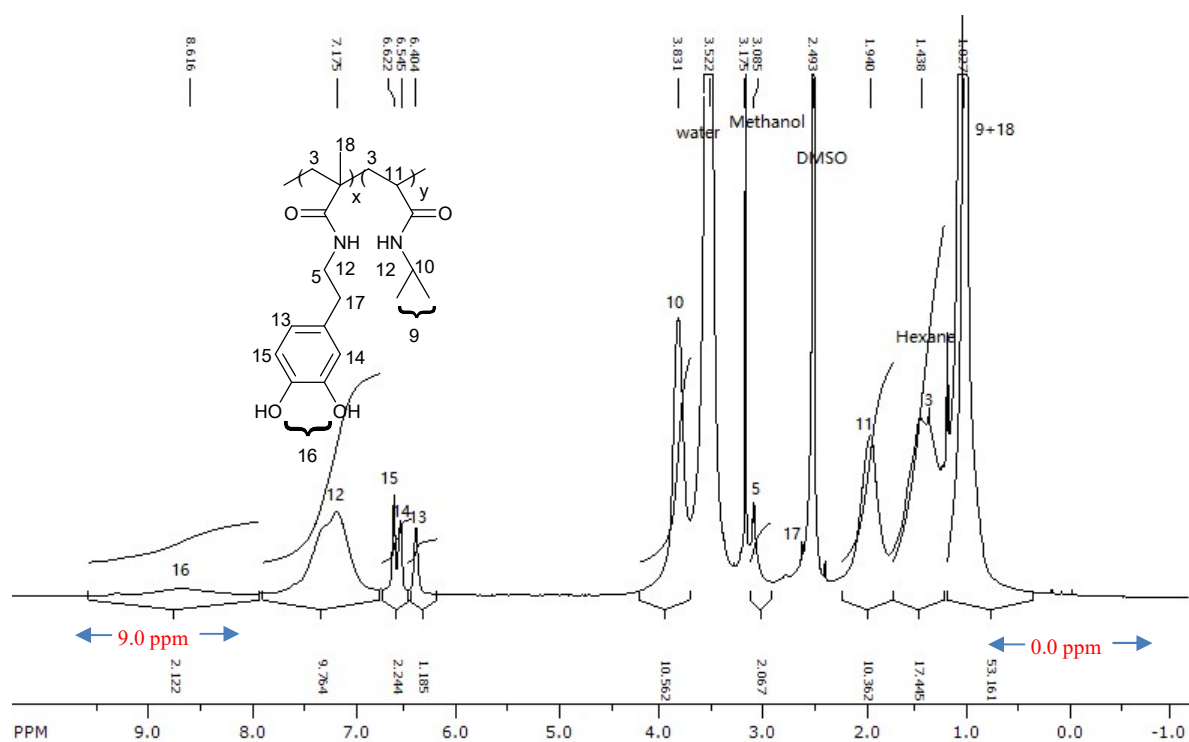

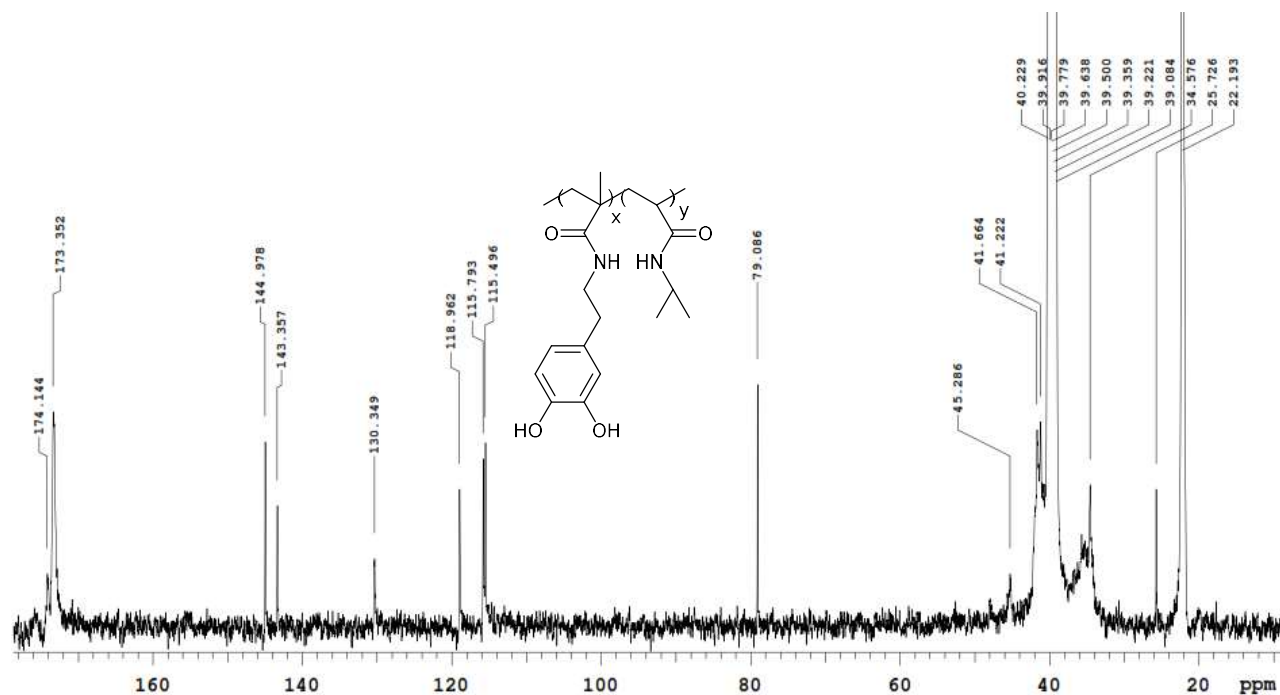**Fig. S6** ^{1}H NMR spectrum of P(DMA-*co*-NIPAM) in DMSO-d6 at 25 °C.

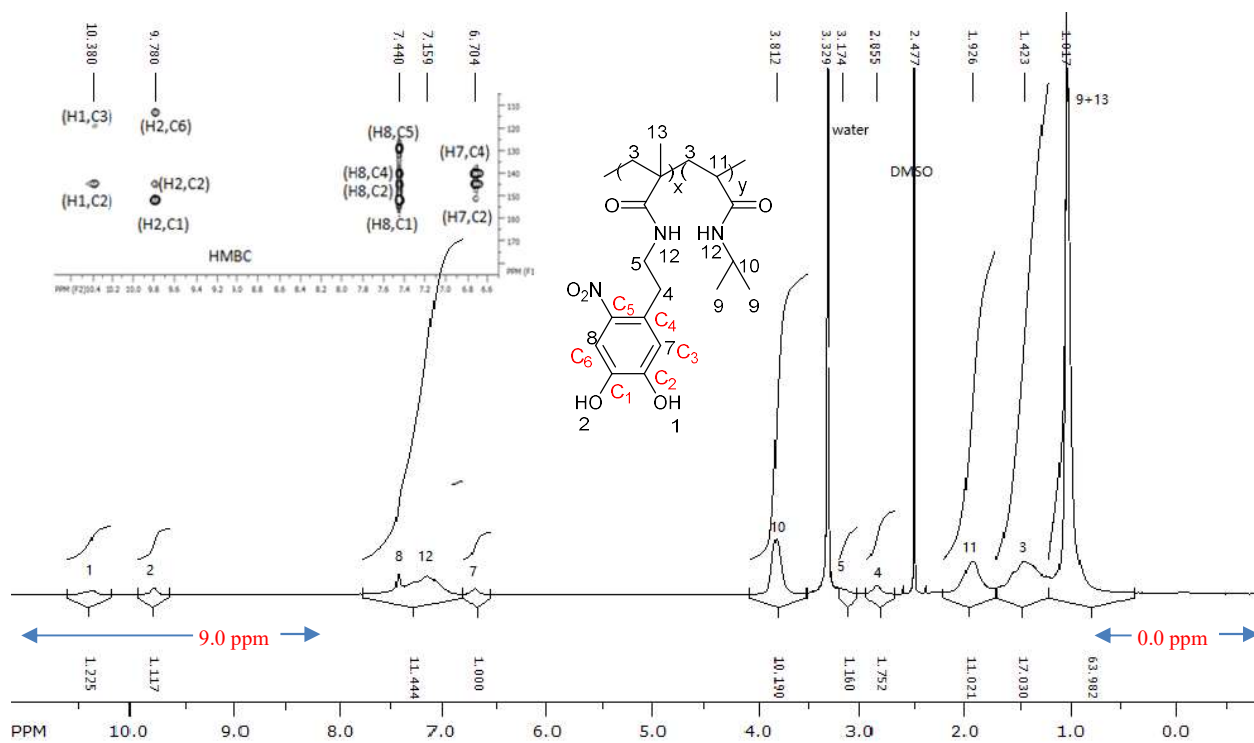**Fig. S7** ^{13}C NMR spectrum of P(DMA-*co*-NIPAM) in DMSO-d6 at 25 °C.

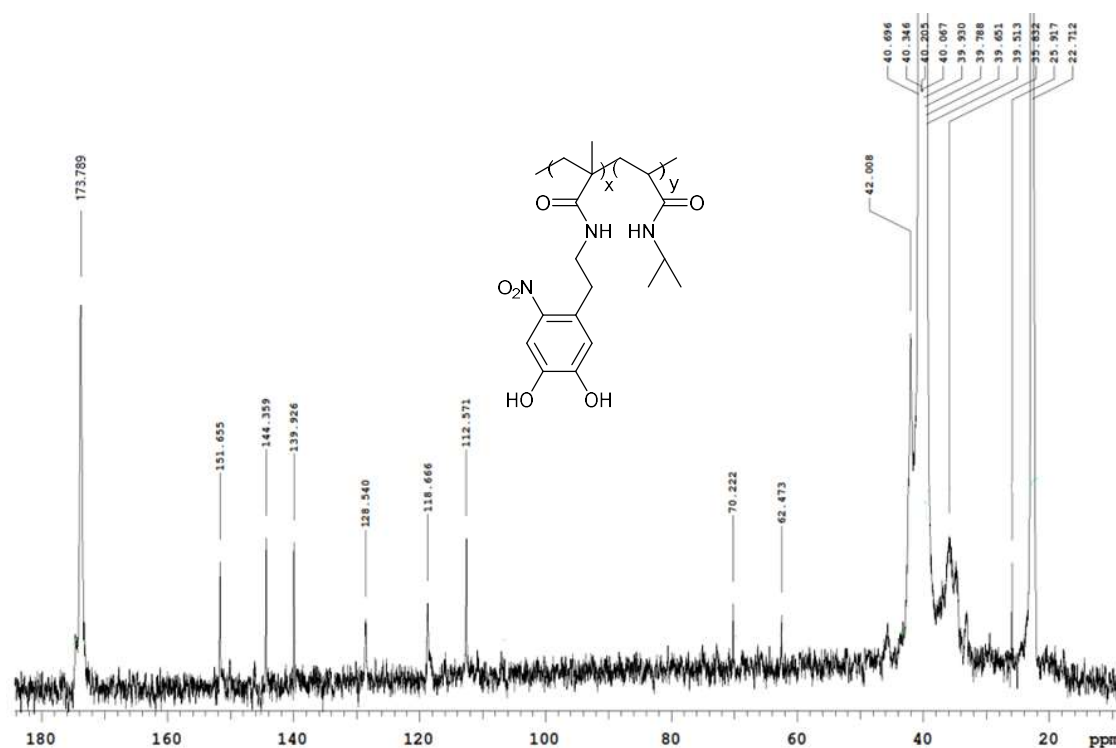**Fig. S8** ^{1}H NMR and ^{1}H-^{13}C HMBC spectra of P(*N*DMA-*co*-NIPAM) in DMSO-d6 at 25 °C.

Fig. S9 ¹³C NMR spectrum of P(*N*DMA-*co*-NIPAM) in DMSO-d6 at 25 °C.
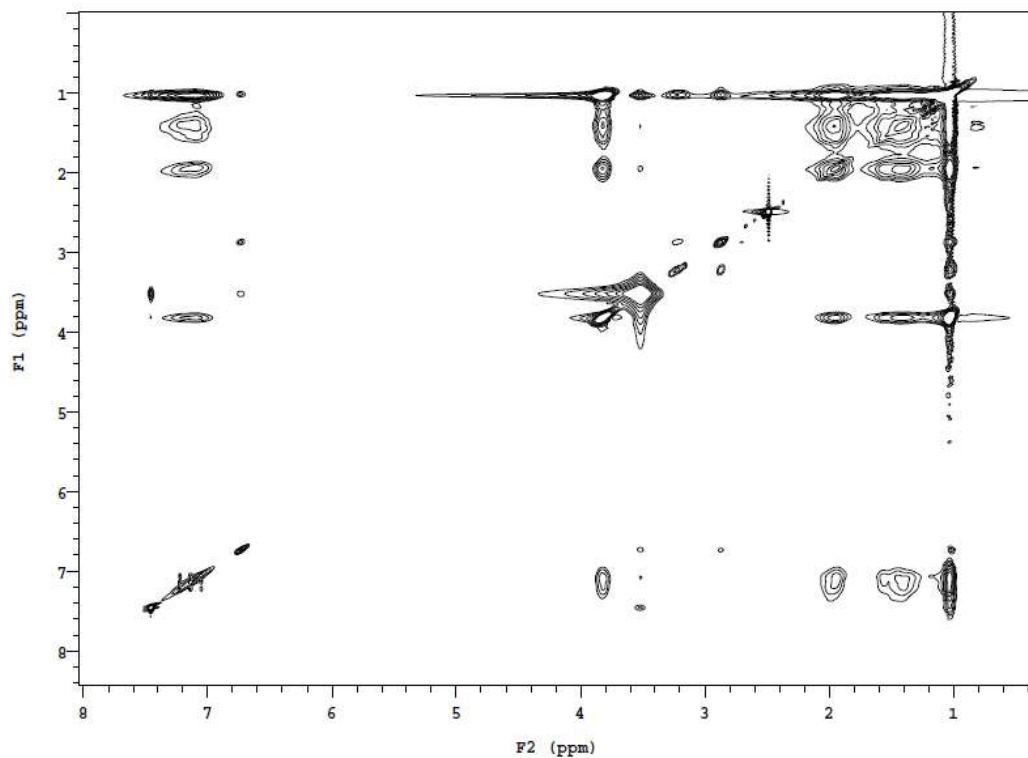

Fig. S10 2D NOESY NMR spectrum of P(*N*DMA-*co*-NIPAM) in DMSO-d6 at 40 °C.
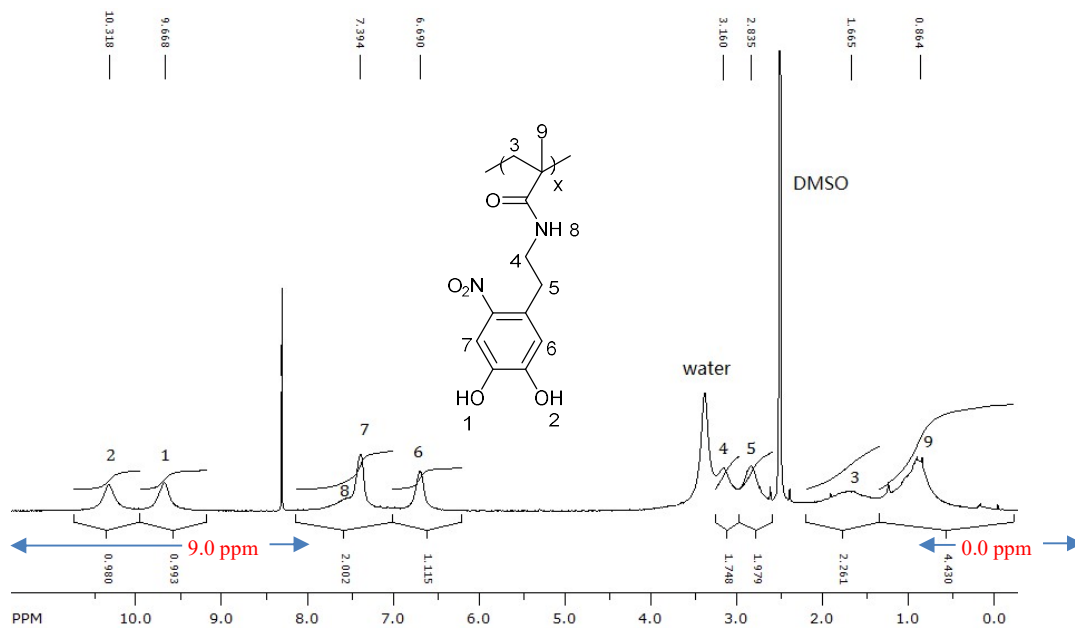
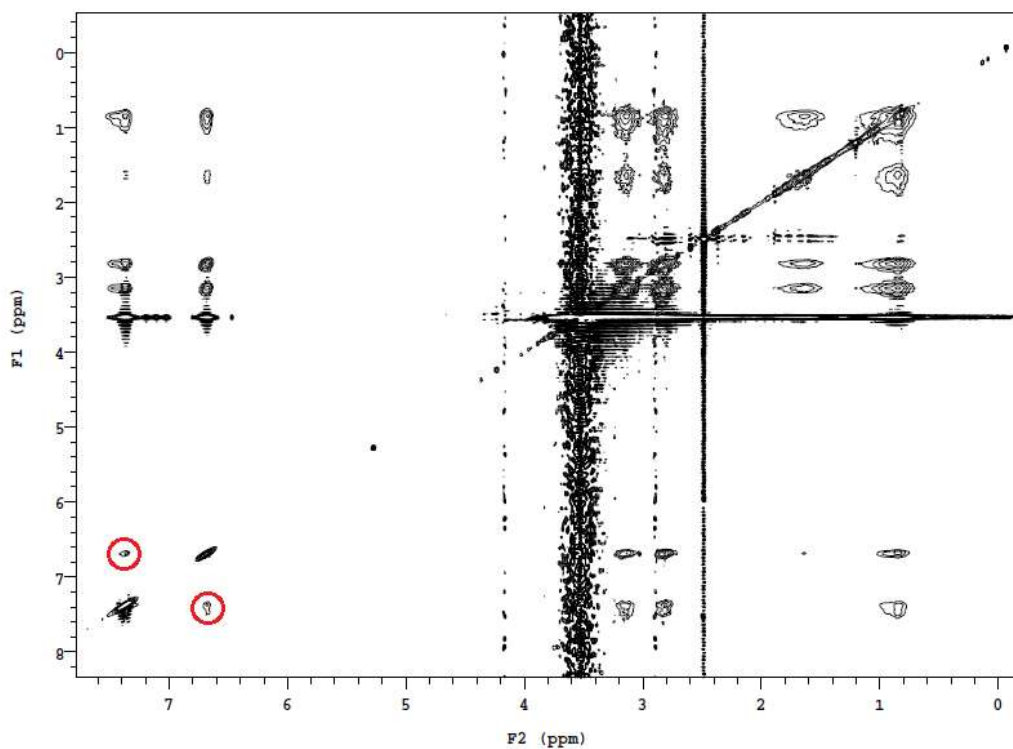**Fig. S11** ^{1}H NMR spectrum of P*N*DMA in DMSO-d6 at 25 °C.

Fig. S12 2D NOESY NMR spectrum of P*N*DMA in DMSO-d6 at 40 °C. The cycled peaks are due to the interaction between the vicinal *N*DMA moieties.

The structure of each compound was confirmed using NMR. In the ^{1}H NMR spectrum of DMA (Fig. S1, ESI†), the signals at 5.6 ppm and 5.3 ppm are corresponding to the vinyl group, and the peaks at 8.7 ppm and 8.6 ppm are related to hydroxyl groups.[1] Capping the hydroxyl groups of DMA using TBDMS was confirmed by the TBDMS signals at 1.0 ppm and 0.2 ppm in the ^{1}H NMR spectrum of *S*DMA (Fig. S3, ESI†), as well as at 18.6 ppm and -3.9 ppm in the ^{13}C NMR spectrum of *S*DMA (Fig. S4, ESI†). In the ^{1}H NMR spectrum of P(*S*DMA-*co*-NIPAM), the vinyl peaks of *S*DMA at 5.6 ppm and 5.3 ppm (Fig. S5, ESI†) disappeared. And the ^{1}H NMR (Fig. S6, ESI†) and ^{13}C NMR (Fig. S7, ESI†) spectra of P(DMA-*co*-NIPAM) are consistent with the literature.[2a] According to the ^{1}H NMR spectrum of P*N*DMA (Fig. S11, ESI†), two aromatic signals of *N*DMA moieties appear at 7.5 ppm and 6.7 ppm in the ^{1}H NMR spectrum of P(*N*DMA-*co*-NIPAM) (Fig. S8, ESI†). Combined with the ^{13}C NMR spectrum of P(*N*DMA-*co*-NIPAM) (Fig. S9, ESI†), cross peaks in the HMBC spectrum of P(*N*DMA-*co*-NIPAM) (Fig. S8, ESI†), (10.4 ppm, 144.4 ppm), (10.4 ppm, 118.7 ppm), (9.8 ppm, 151.7 ppm), (9.8 ppm, 144.4 ppm) and (9.8 ppm, 112.6 ppm), confirm the hydroxyl peaks at 10.4 ppm and 9.8 ppm in ^{1}H dimension.

The PDI and $\overline{M_n}$ were obtained from GPC. The GPC sample concentration is about 1-2 mg/mL in THF stabilized by butylated hydroxytoluene (BHT). As shown by the GPC graph (Fig. S13), the peaks of polymer-5% are at about 8.0-8.2 min with a similar shape. The $\overline{M_n}$ of copolymers is about 14.5 KDa-17.0 KDa. The peak of BHT at 11.4 min and other small molecule peaks closely follow the polymer peaks. The negative air peaks appear after 12 min, not shown here. P(*S*DMA-*co*-NIPAM)-5% shows a broader peak starting from about 7 min, which overlaps with the peaks of BHT and other solvents. The tail of this broad peak results from the small molecules including oligomers, DMF and hexanes, which cannot be removed completely in purification of P(*S*DMA-*co*-NIPAM)-5% using hot hexanes in a Soxhlet apparatus. After deprotection, the obtained P(DMA-*co*-NIPAM)-5% and P(*N*DMA-*co*-NIPAM)-5% have narrower peaks in the range of about 7-10min, resulting from the loss of some small molecules, during polymer precipitation using hydrochloric acid. In the meantime, the PDI decreases from 1.7 to 1.4-1.5. Similar PDI and $\overline{M_n}$ indicate that the same purification protocol resulting in similar catcholic and nitro copolymers.

Table S1 Compositions, $\overline{M_n}$ and PDI of copolymers

	mole % of DMA or *N*DMA in copolymers[a]	$\overline{M_n}$[b] (KDa)	PDI[b]	DP[b]
P(**S**DMA-*co*-NIPAM)-5%	5 %	14.5	1.7	
P(DMA-*co*-NIPAM)-5%	5 %	15.5	1.4	131
P(*N*DMA-*co*-NIPAM)-5%	4 %	17.0	1.5	142
P(**S**DMA-*co*-NIPAM)-10%	10 %	14.7	1.8	
P(DMA-*co*-NIPAM)-10%	10 %	16.5	1.4	133
P(*N*DMA-*co*-NIPAM)-10%	9 %	15.5	1.9	123

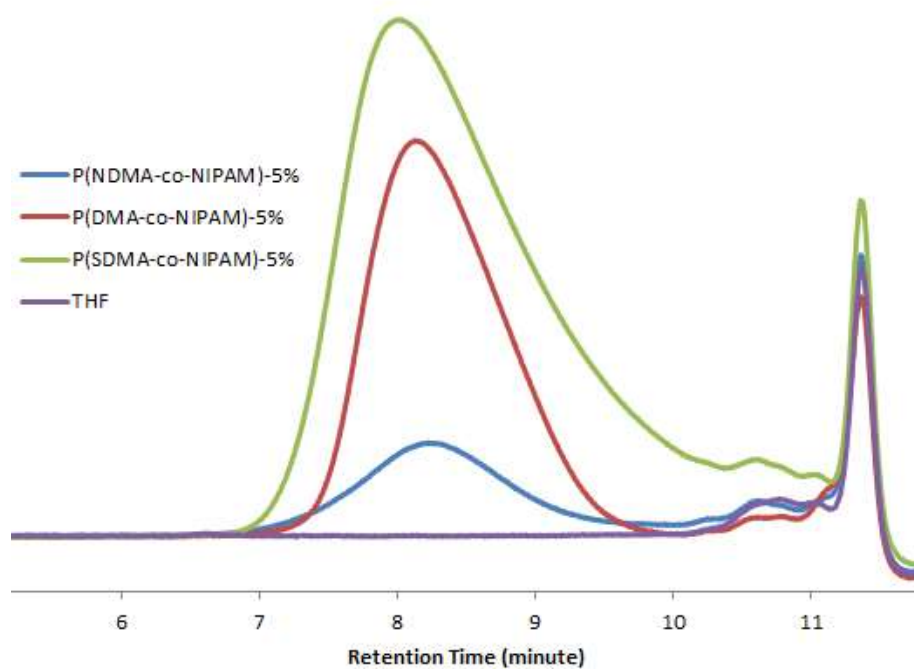[a] From ^{1}H NMR. [b] From GPC.

Fig. S13 GPC traces of copolymer-5%.

3. Preparation of Fe₃O₄ Nanoparticles

In a typical Fe_3O_4 preparation procedure,[3] 3.25 g of $FeCl_3.6H_2O$ (7.2 mmol) was dissolved in 100 mL of water with N_2 bubbling. Subsequently, 0.25 g of Na_2SO_3 (2.0 mmol) in 5 mL of water was added into the $FeCl_3$ solution. After N_2 bubbled for 30 min, the temperature was raised to 70 °C. Then, 20 mL of concentrated ammonia was diluted into 40 mL of water and injected to the reaction solution. The mixture was stirred for another 30 min at 70 °C. Fe_3O_4 particles were collected by a magnet and washed with water and methanol. The particles were kept in N_2 flushed methanol for future use.
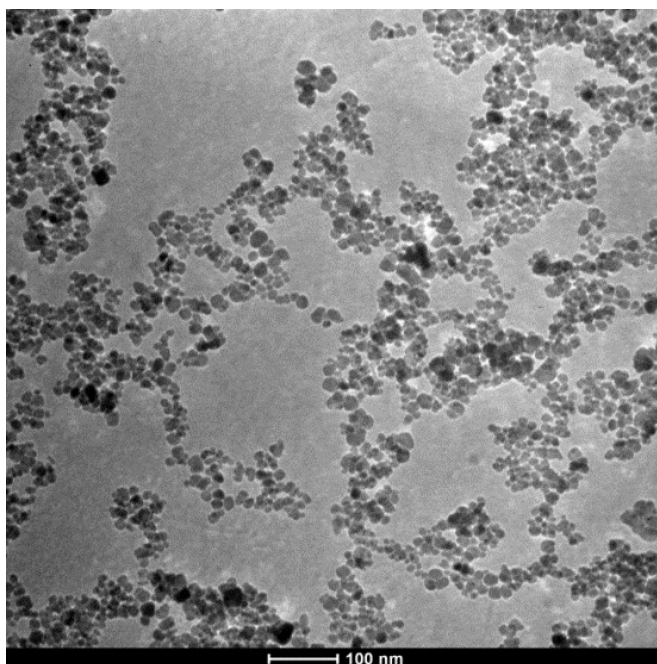

Fig. S14 The TEM image of Fe_3O_4 NPs. The size of the NPs is found to be about 15 nm in diameter on average with irregular shapes. The size measurement is based on 100 randomly selected NPs using Nano Measurer 1.2 software.
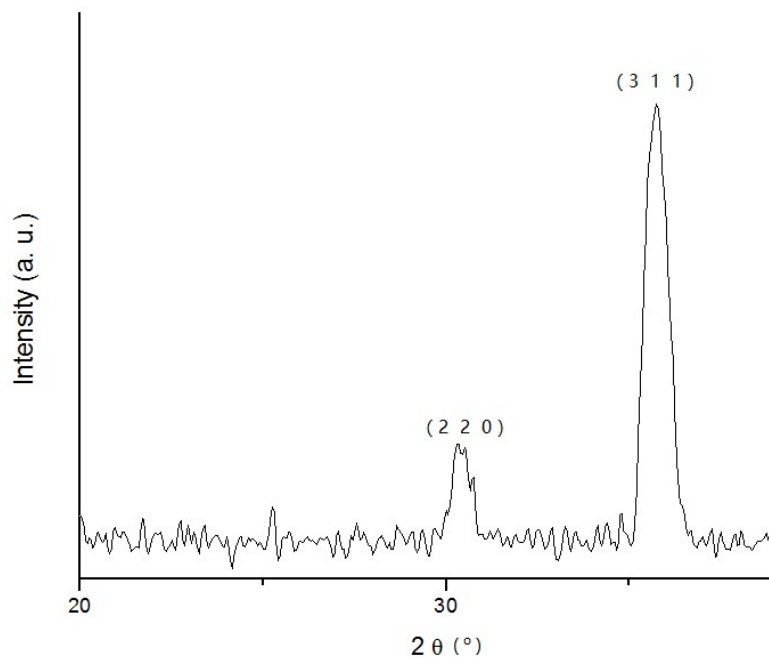
Fig. S15 The WAXS pattern of Fe$_3$O$_4$ $_{NPs}$.

The wide angle X-ray scattering (WAXS) pattern displays two peaks, which correspond to (2 2 0), (3 1 1) of a spinel structure of Fe$_3$O$_4$. The mean size of NPs is also calculated using Debye-Sherrer formula from (3 1 1) peak (Fig. S15). The Debye-Sherrer equation is given as D=0.9λ/βcosθ. D is the average size of NPs; 0.9 is the shape factor; λ is the wavelength of X-ray; β is the line broadening at half of the maximum intensity (radians) and θ is the Bragg angle. For (3 1 1) peak, β=0.01221, θ=17.855 (degree), λ=0.154 nm. The average size of NPs is about 12 nm. This result is consistent with the value obtained from TEM image (Fig. S14).

4. Competitive Binding to Fe$_3$O$_4$ Nanoparticles between Copolymers

P(DMA-*co*-NIPAM) and P(*N*DMA-*co*-NIPAM) in targeted ratios (totally 50 mg) were dissolved in 5 mL of methanol followed by bubbling with N$_2$ for 30 min. The N$_2$ protected Fe$_3$O$_4$/methanol suspension (5 mL, 3 mg/mL) was sonicated for 30 min and injected into polymer mixture under sonication. The mixture was sonicated in an ice bath for additional 30 min and the reaction was monitored using ^{1}H NMR. No degradation of polymers resulting from sonication was observed. Subsequently, the polymer-Fe$_3$O$_4$ composite was separated using a permanent magnet and washed under sonication using N$_2$ flushed methanol (3 × 5 mL). The polymer-Fe$_3$O$_4$ NPs were dispersed in 1 mL of methanol and flushed with N$_2$ in a dry ice bath for 15 min. Then 2 mL of N$_2$ flushed concentrated HCl/ascorbic acid (2 g of ascorbic acid) was added dropwise into the polymer-Fe$_3$O$_4$ suspension in an ice bath. Once Fe$_3$O$_4$ $_{NPs}$ were dissolved, 8 mL of water (N$_2$ flushed) was added to precipitate the polymer out immediately. The polymer was collected by centrifugation and purified by dissolving in methanol and reprecipitating with HCl (pH=2) three times, followed by rinsing using water and diethyl ether. The obtained polymer was dried in a vacuum at room temperature overnight before ^{1}H NMR measurement.

Table S2 Monitoring polymer ratios using ^{1}H NMR in the supernatant of the competitive binding reaction suspensions during sonication[a]

Sonication time	*N*DMA:DMA (The mole ratio between P(*N*DMA-*co*-NIPAM) and P(DMA-*co*-NIPAM) in supernatant)				
	Polymer-5%			Polymer-10%	
0 min (Starting ratio)	0.122	0.213	0.556	0.109	0.189
5 min	0.094±0.022	0.206±0.012	0.463±0.033	0.117±0.003	0.189±0.017
10 min	0.076±0.003	0.199±0.012	0.431±0.040	0.077±0.033	0.189±0.021
20 min	0.077±0.015	0.193±0.029	0.380±0.017	0.078±0.001	0.177±0.040
30 min	0.067±0.016	0.185±0.014	0.377±0.036	0.073±0.002	0.155±0.045

[a] The supernatant samples for the measurement of polymer ratio using ^{1}H NMR were kept on a magnet to remove Fe$_3$O$_4$ $_{NPs}$.

Table S3 EnF calculated based on the initial weight of each polymer, the total weight loss from TGA and the polymer ratio on the surface of Fe$_3$O$_{4\ NPs}$ from ^{1}H NMR[a, b]

Catechol % in polymer	Initial Feed of Copolymers			At reaction equilibrium								
	A	B	C	D	E	F	G	H	I	J	K	L
	NDMA/DMA (mole ratio) in reaction solution[c]	P(DMA-co-NIPAM) weight in reaction solution (mg)	P(NDMA-co-NIPAM) weight in reaction solution (mg)	Total Wt. % of polymers on Fe$_3$O$_4$ from TGA	Polymer mixture weight on Fe$_3$O$_4$ from TGA (mg)[d]	NDMA/DMA (mole ratio) on Fe$_3$O$_4$ from ^{1}H NMR	P(NDMA-co-NIPMA) weight on Fe$_3$O$_4$ from TGA (mg) [E× F/(F+1)]	P(DMA-co-NIPMA) weight on Fe$_3$O$_4$ from TGA (mg) (E-G)	P(DMA-co-NIPMA) weight in supernatant (mg) (B-H)	P(NDMA-co-NIPMA) weight in supernatant (mg) (C-G)	NDMA/DMA (mole ratio) in supernatant from the concentration of polymers (J/I)	EnF (F/K)
5%	0.122	44.5	5.4	8.3±0.5	1.4	2.8±1.5	1.0	0.4	44.2	4.4	**0.10**	**28**
5%	0.213	41.2	8.7	11±1.1	1.9	8.0±0.8	1.7	0.2	41.0	7.1	**0.17**	**47**
10%	0.556	32.1	17.8	9.8±0.5	1.6	15.4±3.9	1.5	0.1	32.0	16.3	**0.51**	**30**
5%	0.109	45.0	4.9	10.9±1.8	1.8	3.1±0.5	1.4	0.4	44.7	3.5	**0.08**	**39**
5%	0.189	42.0	7.9	10.6±2.3	1.8	6.6±2.6	1.6	0.2	41.8	6.4	**0.15**	**44**

[a] All data are average results from triplicate experiments. All error bars are standard deviations. [b] P(DMA-co-NIPMA) and P(NDMA-co-NIPAM) are assumed to have the same Mn. [c] The mole ratios were calculated using ^{1}H NMR. [d] The input weight of Fe$_3$O$_{4\ NPs}$ was 15 mg.
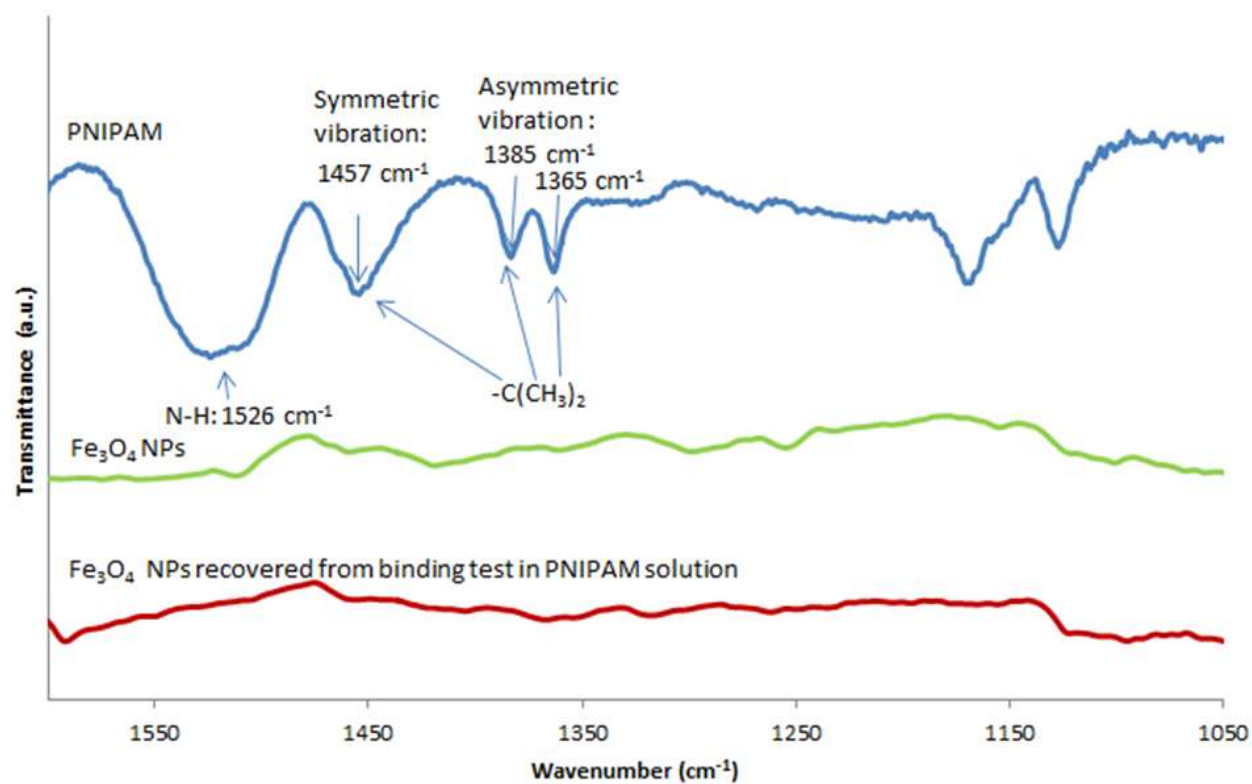
Fig. S16 FT-IR spectra of PNIPAM, $Fe_3O_{4\ NPs}$ and $Fe_3O_{4\ NPs}$ recovered from the binding test in PNIPAM solution.
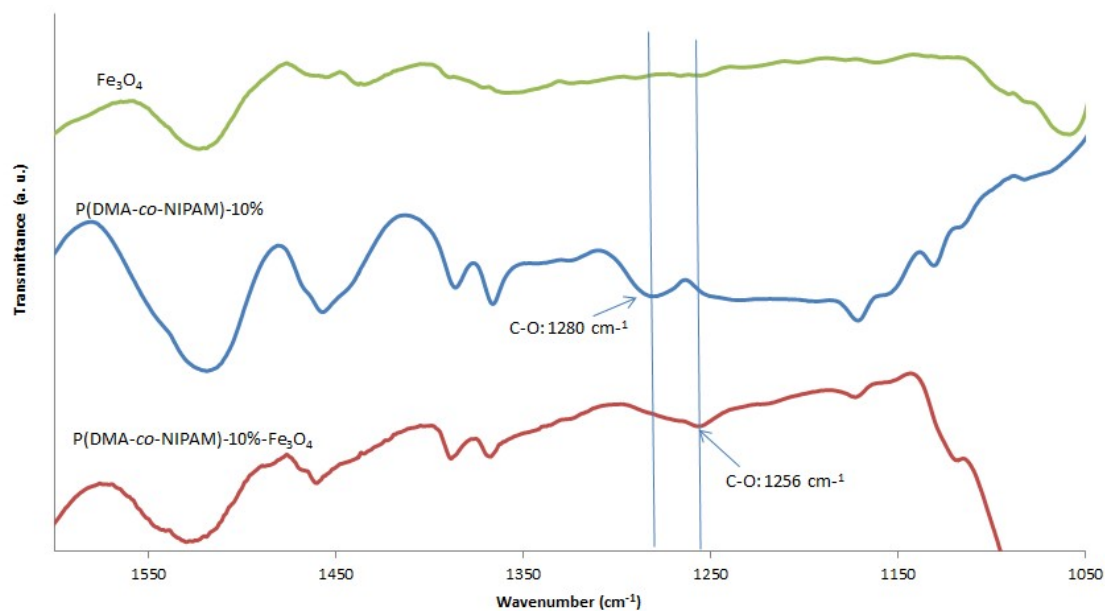
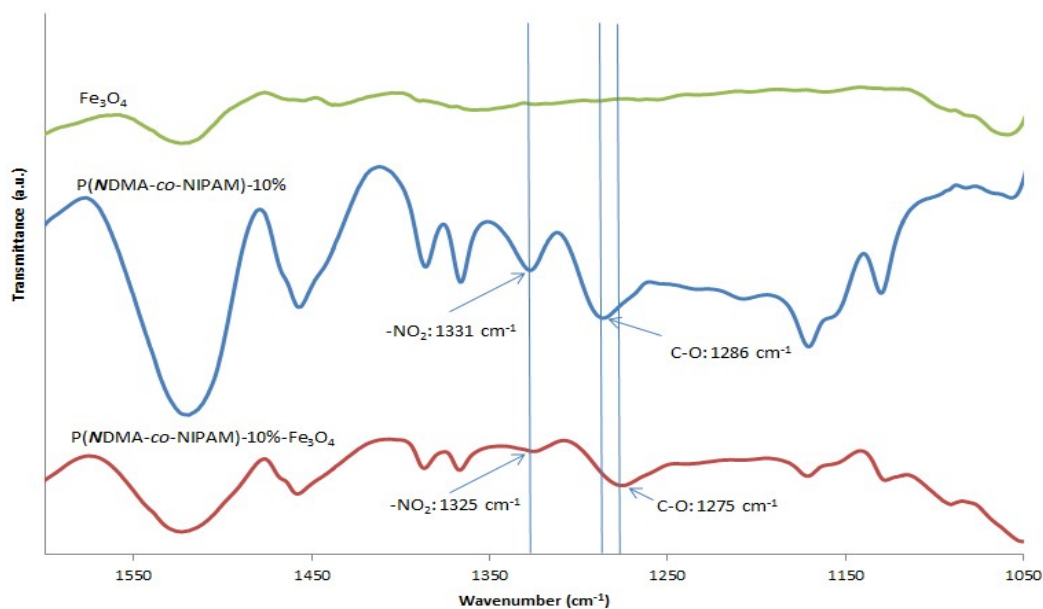**Fig. S17** FT-IR spectra of P(DMA-*co*-NIPAM)-10%, $Fe_3O_{4\ NPs}$ and P(DMA-*co*-NIPAM)-10%-Fe_3O_4 composite.

Fig. S18 FT-IR spectra of P(*N*DMA-*co*-NIPAM)-10%, Fe_3O_4 $_{NPs}$ and P(*N*DMA-*co*-NIPAM)-10%-Fe_3O_4 composite.
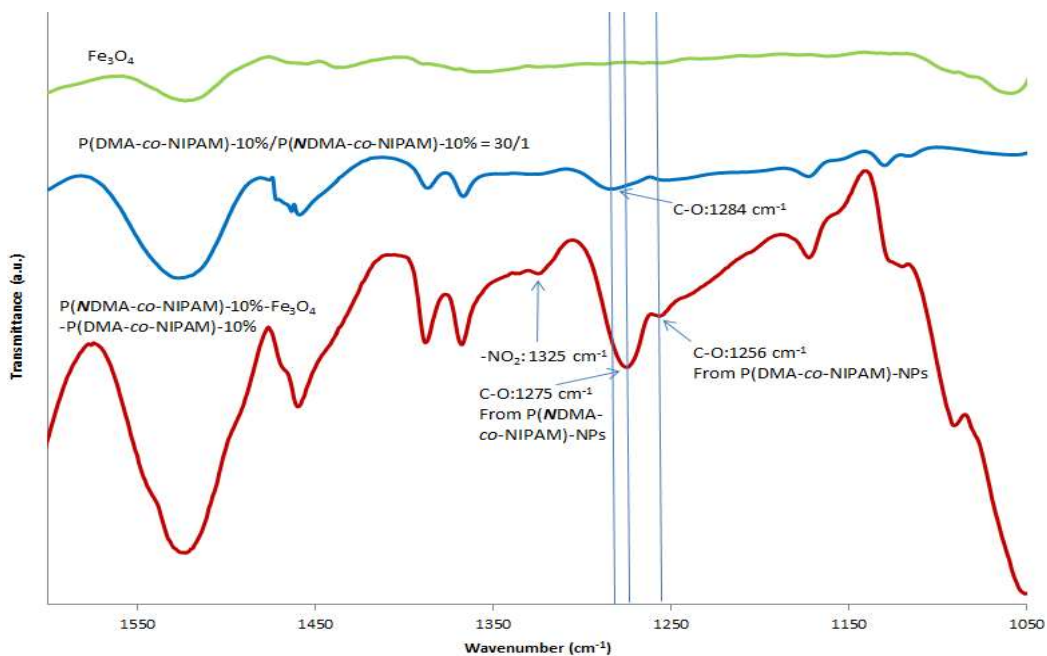
Fig. S19 FT-IR of P(*N*DMA-*co*-NIPAM)-10%/P(DMA-*co*-NIPAM)-10% (1/30) mixture, Fe_3O_4 $_{NPs}$ and P(*N*DMA-*co*-NIPAM)-10%-Fe_3O_4-P(DMA-*co*-NIPAM)-10% (coating of Fe_3O_4 $_{NPs}$ using polymer mixture).

S20

5. Comparison of the Binding Affinity of Copolymers to 4-Fluorophenylboronic Acid

A solution of 0.20 mg/mL of FPBA was prepared in 0.1 M of PBS (pH=6.5, 7.4 and 8.5) (solution A). Then a diol of choice (catechol, 4-nitrocatechol, the non-nitro or nitro copolymer) in excess (about 2-3 equiv.) was dissolved in FPBA solution (solution B). The resulted pH values of solution A and solution B were tuned to the corresponding pH, if there was any deviation. Solution A and solution B were mixed with different ratios (about 500 µL, 10 % D_2O) in NMR tube to determine the binding constants. Each sample was mixed using Vortex for 3 minutes before NMR measurement. Spectra were collected every 5-10 minutes in 30-40 minutes to make sure equilibrium has been established, and trimethylsilylpropanoic acid (TSP) was used as reference calibration at close to the LCST of copolymers, 20 °C or 15 °C. The electrode of pH meter was calibrated using two standard buffer solutions which were close to the targeted pH values.

The determination of binding constants was performed by plotting [boronate] versus [FPBA][Diol] (Fig. S24-S27, ESI†).

Table S4 Binding constants of diols to FPBA[a]

pH	Binding constants (M^{-1})			Percentage of catecholate or nitrocatcholate (%)[b]		
	6.5	7.4	8.5	6.5	7.4	8.5
Catechol	170	1480	8220	0.16	1.2	14
4-Nitrocatechol	3090	6600	8170	39	83	98
P(DMA-*co*-NIPAM)-5%	90	550	2530	-	-	-
P(*N*DMA-*co*-NIPAM)-5%	2120	2830	-	-	-	-

[a] Binding constants were determined in 0.10 M PBS solution containing 10 % of D_2O using ^{1}H NMR. The binding constants at pH 6.5 for polymer-5% were measured at 15 °C and all other binding constants were measured at 20 °C. [b] The calculation is based on the reported pK$_{a1}$ values in reference.[4] Catechol, pK$_{a1}$=9.27; 4-nitrocatechol, pK$_{a1}$=6.69.
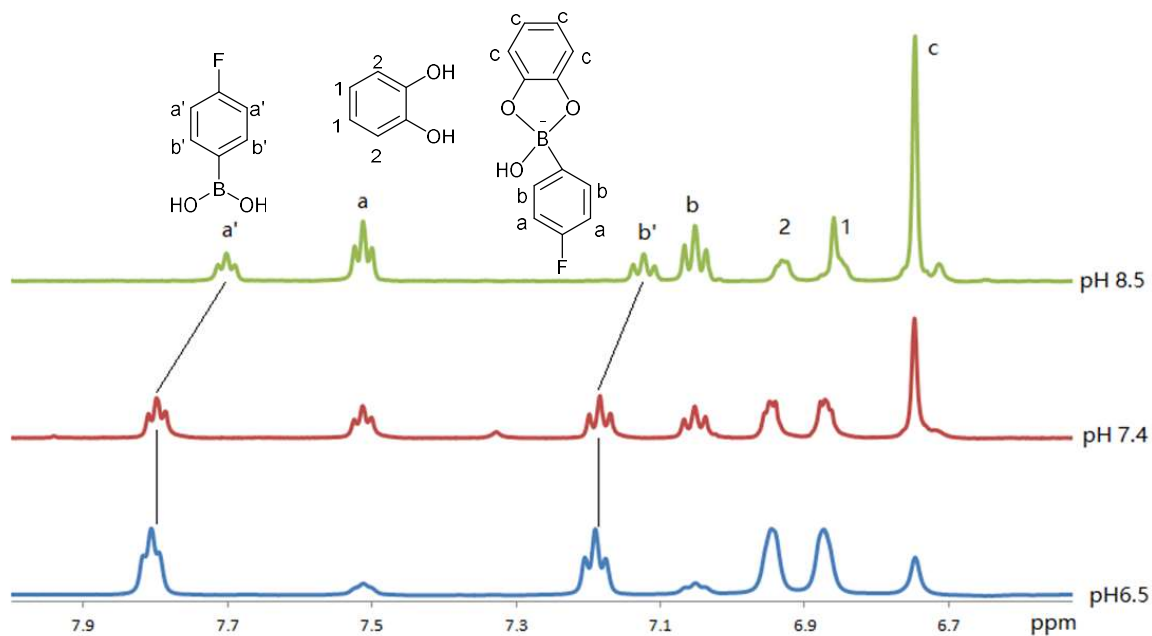
Fig. S20 ¹H NMR spectra of catechol boronate ester formation at different pH with a constant starting ratio of catechol to FPBA (1:1) at 20 ℃.
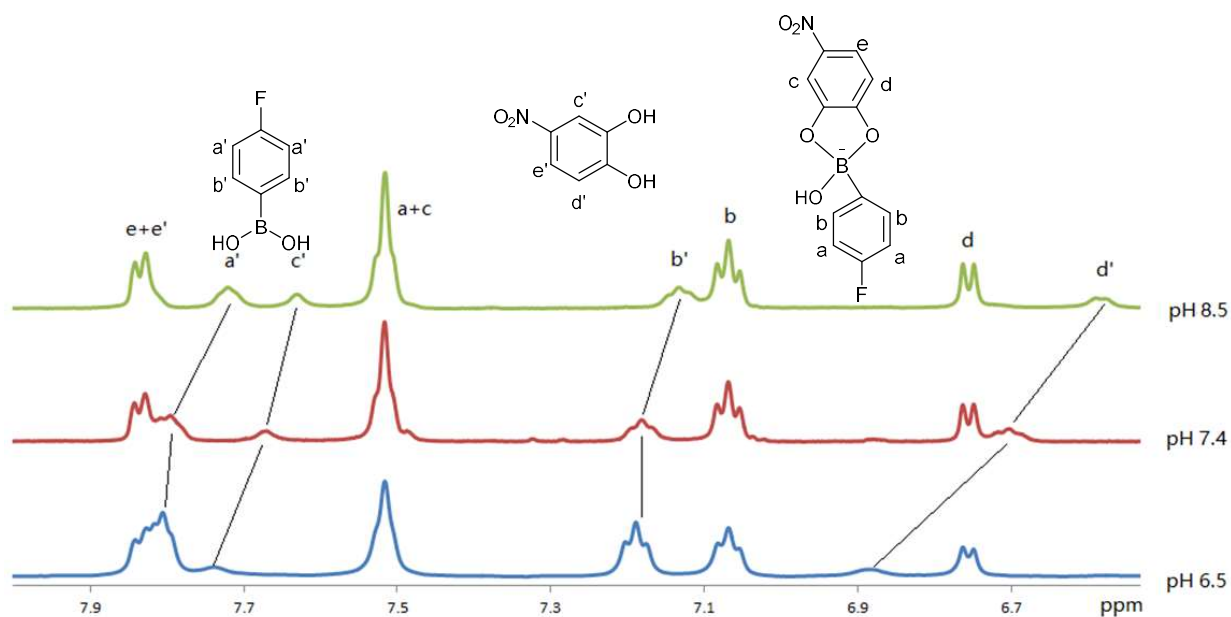

Fig. S21 ¹H NMR spectra of nitrocatechol boronate ester formation at different pH with a constant starting ratio of 4-nitrocatechol to FPBA (1:1) at 20 ℃.
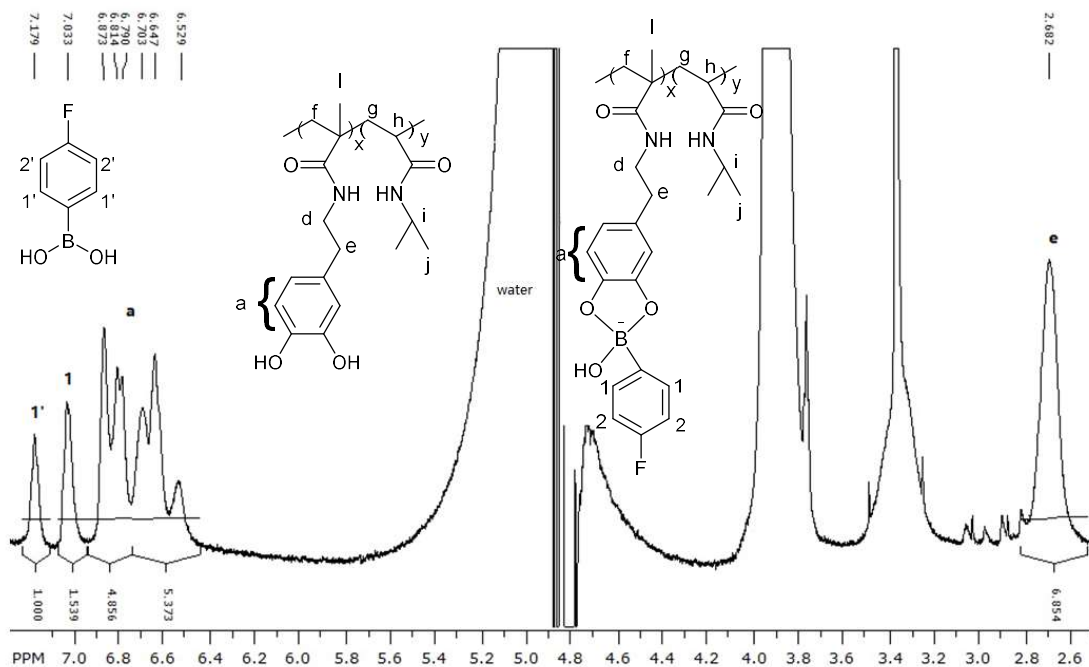
Fig. S22 Selected ^{1}H NMR spectrum of boronate formation between P(DMA-*co*-NIPAM)-5% and FPBA at pH 7.4 at 20 °C.
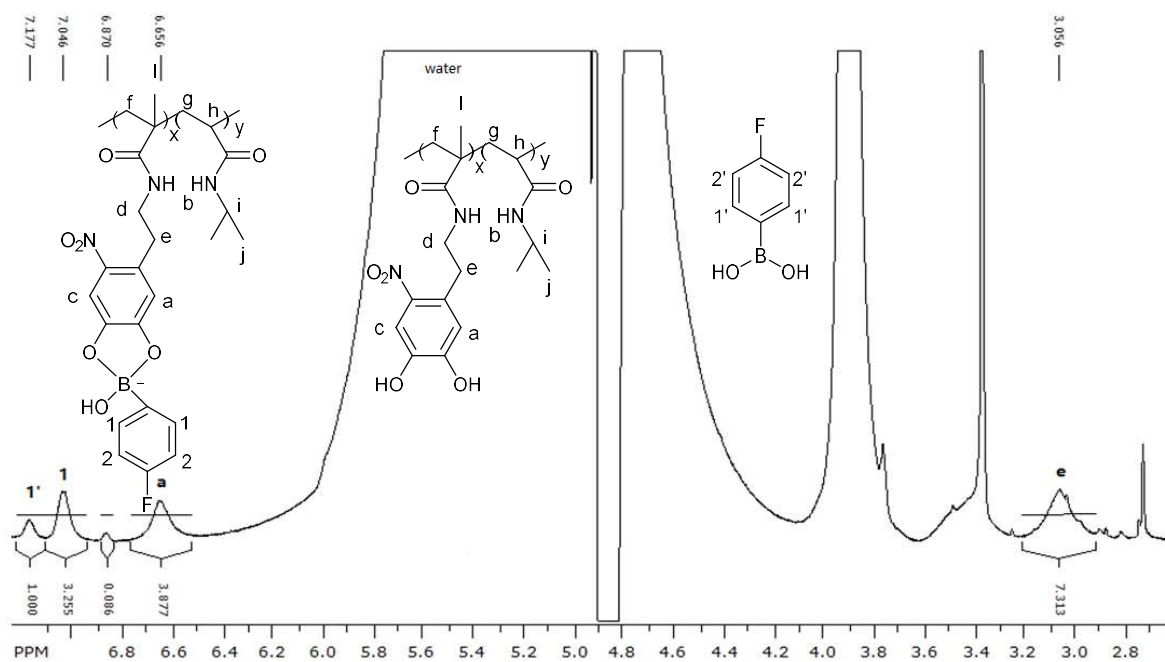

Fig. S23 Selected ^{1}H NMR spectrum of boronate formation between P(*N*DMA-*co*-NIPAM)-5% and FPBA at pH 7.4 at 20 °C.
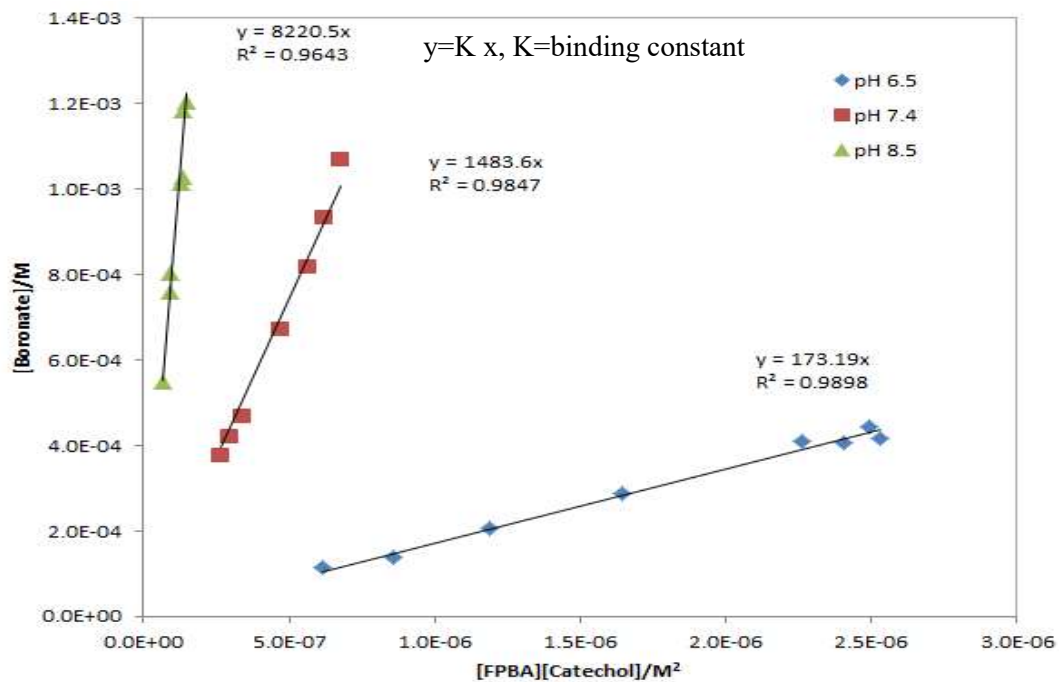
Fig. S24 Determination of binding constants between catechol and FPBA at 20 °C.
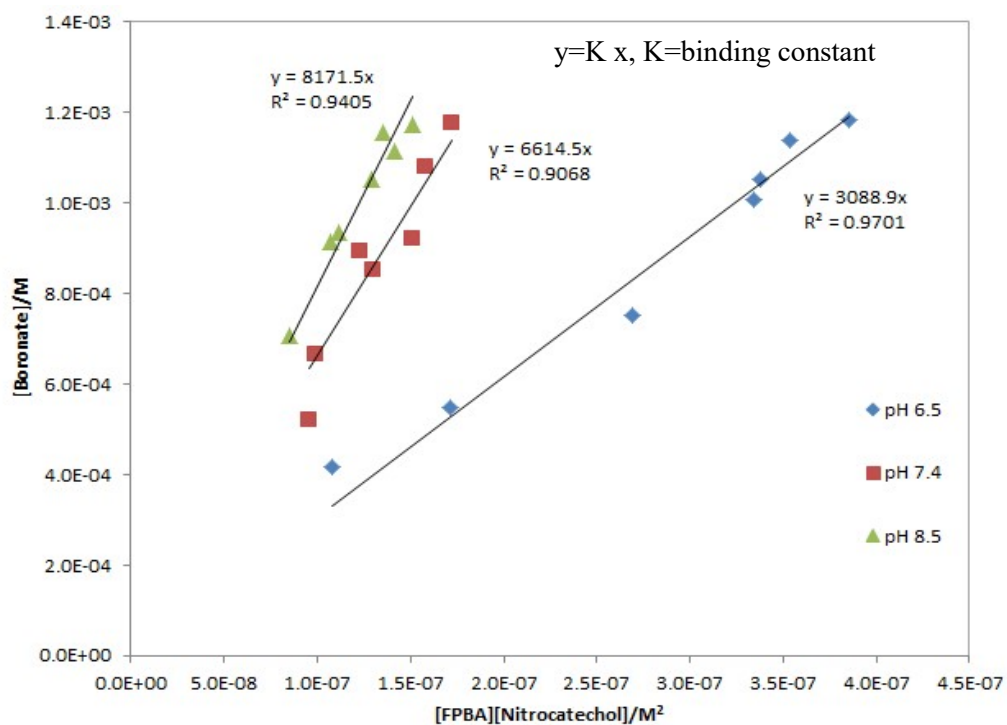

Fig. S25 Determination of binding constants between 4-nitrocatechol and FPBA at 20 °C.
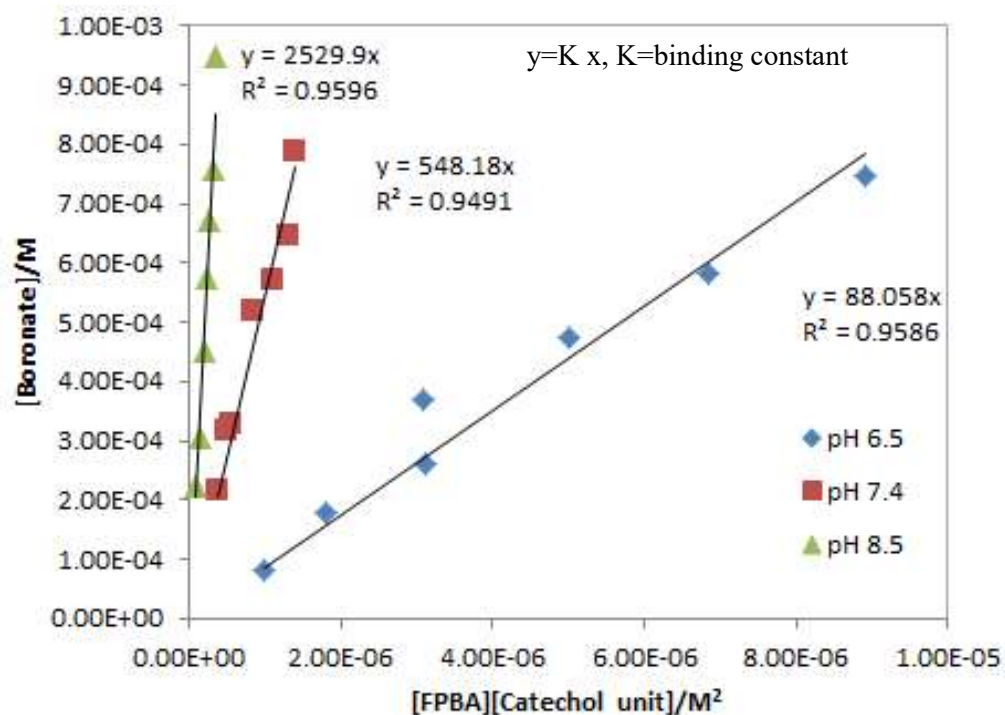
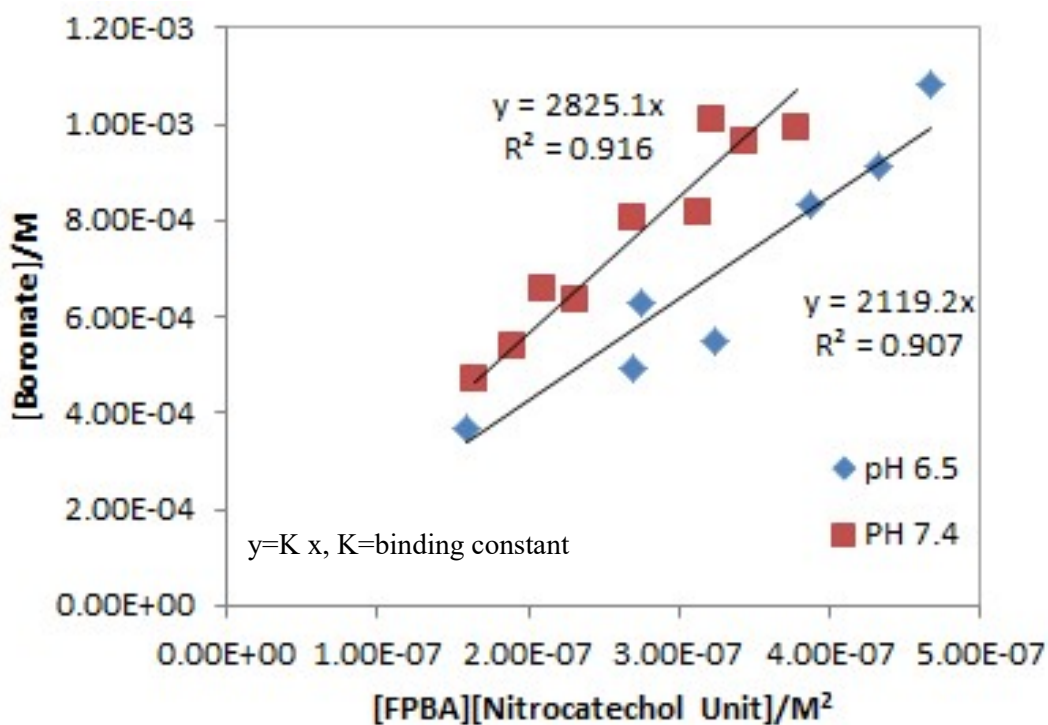**Fig. S26** Determination of binding constants between P(DMA-*co*-NIPAM)-5% and FPBA.

Fig. S27 Determination of binding constants between P(*N*DMA-*co*-NIPAM)-5% and FPBA.

6. References

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