Electronic Supplementary Material (ESI) for Journal of Materials Chemistry A.

Electronic Supplementary Information

Eosin Y Functionalized Tertiary Amines-Bearing Interpenetrating Polymer Networks for Heterogeneous Catalysis of Logic-Controlled Oxygen-Tolerant Radical Polymerization

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Experiment Section

Materials

Eosin Y disodium salt (EY, >85%), 3-bromopropylamine hydrobromide (98%), 1,2-bis(2-aminoethoxy)ethane (BAE, 98%), 3-(diethylamino)propylamine (DEAPA, ≥99%), poly(ethylene glycol) diglycidyl ether (PGE, M_n = 500 g/mol), methoxy poly(ethylene oxide)-2-(dodecylthiocarbonothioylthio)-2-methylpropionate (PEG-DDMAT, M_n = 1100 g/mol), bovine serum albumin lyophilized powder (BSA, M_n ≈ 6600 g/mol, ≥96%) and tris(2-carboxyethyl)phosphine (TCEP, ≥98%) were purchased from Sigma-Aldrich or Alfa-Aesar and used as received unless otherwise indicated. All liquid monomers including *N,N*-dimethylacrylamide (DMA, 99%), *N,N*-diethylacrylamide (DEA, 99%), 4-acryloylmorpholine (AMP, 98%), hydroxyethyl acrylate (HEA, 96%), methyl acrylate (MA, 99%), *tert*-butyl acrylate (*t*BA, ≥99%), glycidyl methacrylate (GMA, ≥97%), pentafluorophenyl methacrylate (PFMA, 95%), tetra(ethylene glycol) diacrylate (TEGDA, 97%) and poly(ethylene glycol) methyl ether methacrylate (PEGMA, M_n = 500 g/mol) were purchased from Sigma-Aldrich Chem. Co. and purified by percolating over an inhibitor-removal column prior to use. *N*-isopropylacrylamide (NIPAM, 97%) was recrystallized twice from toluene/hexane (7:3, v/v). The radical initiator, 2,2′-azobis(2-methylpropionitrile) (AIBN, 97%) was purchased from Kanto Chemical Co. (Tokyo, Japan) and was recrystallized from anhydrous ethanol. 2-(Butyltrithiocarbonothioylthio)propionic acid (BTPA) and 2-(pyridine-2-yldisulfanyl)ethyl 2-(((dodecylthio)carbonthioyl)thio)propanoate (PDP) were prepared according to procedures described in the literature.[1-4]

Instrumentation

Nuclear magnetic resonance (NMR) spectroscopy and gel permeation chromatography (GPC) were used to characterize the molecular weights and chemical structures of the synthesized polymers. ^{1}H NMR spectroscopy were recorded on a Bruker ARX operating at 400 MHz for ^{1}H using deuterated dimethyl sulfoxide (DMSO-d_6) and deuterated chloroform ($CDCl_3$) as the solvents and an internal reference with chemical shifts (δ) reported in ppm. GPC analyses were performed on a Waters GPC system equipped with an isocratic pump model 1515, a differential refractometer model 2414, a dual-wavelength UV detector model 2487 and Styragel columns. The number-average molecular weight ($M_{n,GPC}$) and polydispersity index ($Đ = M_{w,GPC}/M_{n,GPC}$) were measured with narrow molecular weight distribution poly(methyl methacrylate) (PMMA) or poly(ethylene oxide) as the standards, coupled with tetrahydrofuran (THF), *N,N*-dimethylformamide (DMF) or water as the eluent at a flow rate of 1.0 mL/min.

The thermal stability of the gels was investigated by thermogravimetric analysis (TGA). The samples were heated from 40 ºC to around 700 ºC with a heating rate of 10 ºC/min under a dry nitrogen atmosphere in a thermal analyzer (TGS-II, PerkinElmer). Surface composition of the gels was investigated by X-ray photoelectron spectroscopy (XPS) on a Kratos AXIS Ultra DLD spectrometer sourcing with a monochromatized Al Kα X-ray source (1468.71 eV photons).

The mass of the completely dry network (W_d) was recorded and then immersed in an aqueous medium of prescribed pH. The surface of the gels was dried with a filter paper, and the mass of the swollen gels was recorded (W_s). The data reported were averaged

measurements from at least five similar gel samples, and the standard derivations were within ± 10%. The solution pH was determined by a Mettler Toledo Delta 320 pH meter. This process was repeated until the sample reached a constant weight in the determination of equilibrium swelling ratio (ESR). The ESR of polymer networks were determined gravimetrically using following relation:

$$\mathrm{ESR} = [(W_s - W_d)/W_d] \times 100\% \quad (1)$$

Synthesis of EY-NH_2

EY (2.08 g, 3.0 mmol), 3-bromopropylamine hydrobromide (985 mg, 4.5 mmol) and DMF (15 mL) were successively added to a Schlenk tube.[5,6] The reaction mixture was deoxygenated by sparging argon for 20 min. The reaction was allowed to proceed at 80 ºC for 12 h under vigorous stirring. After that, the reaction was quenched by immersing the Schlenk tube into an icy water bath, followed by precipitating in a mixed solution of diethyl ether and deionized water (v/v, 1:1) to eliminate any nonreacted reactants. The purification protocol was repeated twice. The crude product was purified by column chromatography on silica gel to give compound EY-NH_2 as a red solid. Yield: ~85%.

Synthesis of IPN-GEY Gels

Briefly, EY-NH_2 (42.3 mg, 0.06 mmol), PGE (0.6 g, 1.2 mmol), DEAPA (9.4 μL, 0.06 mmol), BAE (78.7 μL, 0.54 mmol) and DMF (1 mL) were successively added to a glass vial. The reaction mixture was deoxygenated by sparging argon for 10 min. The polymerization was allowed to proceed at 70 ºC for 7 h. Argon-purged DMF (0.1 mL) containing HEA (69 μL, 0.6 mmol), TEGDA (9.8 μL, 0.036 mmol) and AIBN (3 mg) was quickly dosed to the glass vial by ultrasonication for 15 min. Afterwards, the

polymerization was allowed to proceed at 75 ºC for another 8 h. After the reaction, the gels were removed from the glass vial and immersed in DMF. DMF solvent was changed about 12 h later, and it was changed for at least five times at 12 h periods. The gels were further immersed into ultrapure water and the solvent was changed for at least five 5 times at 12 h periods. Finally, the IPN-GEY gels was collected via lyophilization. The IPN-GEY gels were cut into small pieces (2×2×2 mm^3 in dry state) and swollen in degassed ultrapure water prior to use.

Synthesis of IPN-ZGEY Gels

Briefly, three pieces of IPN-GEY gels (2×2×2 mm^3 in dry state), PS (0.37 g, 3.0 mmol) and DMF (5 mL) were successively added to a glass vial. The reaction mixture was deoxygenated by sparging argon for 10 min. Then, the modification was allowed to proceed at room temperature for 24 h after being sealed with a rubber septum. Afterwards, the gels were removed from the glass vial and immersed in DMF. DMF solvent was changed about 12 h later, and it was changed for at least five times at 12 h periods. The gels were further immersed into ultrapure water and the solvent was changed for at least five 5 times at 12 h periods. Finally, the IPN-ZGEY gels were collected via lyophilization.

Synthesis of SN-GEY Gels

Briefly, EY-NH_2 (42.3 mg, 0.06 mmol), PGE (0.6 g, 1.2 mmol), DEAPA (9.4 μL, 0.06 mmol), BAE (78.7 μL, 0.54 mmol) and DMF (1 mL) were successively added to a glass vial. The reaction mixture was deoxygenated by sparging argon for 10 min. The polymerization was allowed to proceed at 70 ºC for 12 h. After the reaction, the gels were removed from the glass vial and immersed in DMF. The DMF solvent was changed about

12 h later, and it was changed for at least five times at 12 h periods. The gels were further immersed into ultrapure water and the solvent was changed for at least five 5 times at 12 h periods. Finally, the SN-GEY gels were collected via lyophilization. The SN-GEY gels were cut into small pieces (2×2×2 mm^3 in dry state) and swollen in degassed ultrapure water prior to use.

Synthesis of SN-GHEA Gels

Briefly, HEA (230 μL, 2.0 mmol), TEGDA (32.6 μL, 0.12 mmol), AIBN (5 mg) and DMF (1 mL) were successively added to a glass vial. The reaction mixture was deoxygenated by sparging argon for 10 min. The polymerization was allowed to proceed at 70 ºC for 12 h. After the reaction, the gels were removed from the glass vial and immersed in DMF. The DMF solvent was changed about 12 h later, and it was changed for at least five times at 12 h periods. The gels were further immersed into ultrapure water and the solvent was changed for at least five 5 times at 12 h periods. Finally, the SN-GHEA gels were collected via lyophilization.

General Procedure for the Kinetic Studies of PET-RAFT Polymerization Mediated by IPN-GEY or SN-GEY Gels

A typical PET-RAFT polymerization of DMA in ultrapure water (50 vol%) was performed using varied molar feed ratio of [DMA]:[BTPA] and one piece of IPN-GEY or SN-GEY gels (2×2×2 mm^3 in dry state). The solution pH was monitored using a pH meter and adjusted by slow addition of 0.1 mol/L HCl solution and $NaHCO_3$ powder. After the reaction mixture were placed in a glass vial with a magnetic stirrer and deoxygenated by sparging argon for 20 min, the glass vial was sealed with a rubber septum and irradiated to green LED light (4.8 W, λ_{max} = 520 nm, 1.0 mW/cm^2). After a

certain period, the polymerization was terminated by ceasing the LED light irradiation, purified by dialysis against ultrapure water and collected by lyophilization. To investigate the polymerization kinetics, aliquots of reaction mixtures were withdrawn periodically by argon-purged syringe and analyzed by ^{1}H NMR and GPC measurements. To evaluate the recyclability of the catalysts, the gels were extracted thoroughly with ultrapure water for regeneration.

Following the similar protocol, PET-RAFT polymerization of MA in DMSO (50 vol%) was conducted using a molar feed ratio [MA]:[BTPA] of 200:1 and one piece of IPN-GEY gel (2×2×2 mm^3 in dry state). After the reaction mixture and gels were placed in a glass vial with a magnetic stirrer and deoxygenated by sparging argon for 20 min, the glass vial was sealed with a rubber septum and irradiated under green LED light (4.8 W, λ_{max} = 520 nm, 1.0 mW/cm^2). After a certain period, the polymerization was terminated by ceasing the LED light irradiation and the resultant mixture was quenched by dilution with DMSO, and precipitated into methanol to eliminate any leftover monomers. To investigate the polymerization kinetics, aliquots of reaction mixtures were withdrawn periodically by argon-purged syringe and analyzed by ^{1}H NMR and GPC measurements.

Synthesis of BSA-PDP Macro-CTA

BSA (50 mg) and phosphate buffer solution (pH = 7.0, 9 mL) were introduced into a 25 mL single-necked round bottom flask. The flask was immersed in an ice bath and PDP (53.4 mg, 0.1 mmol) in dry DMSO (1 mL) was added dropwise. Upon completion of the addition, the reaction mixture was kept in the ice-water bath for 1 h and then at room temperature for 12 h. Excessive water was added to the reaction mixture and the BSA

solution were recovered by centrifugation to eliminate any leftover reagents. The raw product was dialyzed against deionized water for 1 day (MWCO 3000 Da). Finally, the BSA-PDP was isolated by lyophilization as a pale-yellow powder. Yield: 72%.

General Procedures for PET-RAFT Polymerization of DMA from BSA-PDP Macro-CTA Mediated by IPN-GEY Gels

A typical PET-RAFT polymerization of DMA in phosphate buffer solution (pH = 7.0, 50 vol%) was performed using [DMA]:[BSA-PDP] molar feed ratio of 1000:1 and one piece of IPN-GEY gel (2×2×2 mm^3 in dry state). After the reaction mixture were placed in a glass vial with a magnetic stirrer and deoxygenated by sparging argon for 20 min, the glass vial was sealed with a rubber septum and irradiated to green LED light (4.8 W, λ_{max} = 520 nm, 1.0 mW/cm^2). After a certain period, the polymerization was terminated by ceasing the LED light irradiation, purified by dialysis against ultrapure water and collected by lyophilization. To investigate the polymerization kinetics, aliquots of reaction mixtures were withdrawn periodically by argon-purged syringe and analyzed by GPC measurements. The residual protein solution was treated with aqueous solution containing TCEP (2.0 mg/mL) and incubated at room temperature for 24 h. Polymer samples were collected by lyophilization and analyzed by ^1H NMR and GPC measurements.

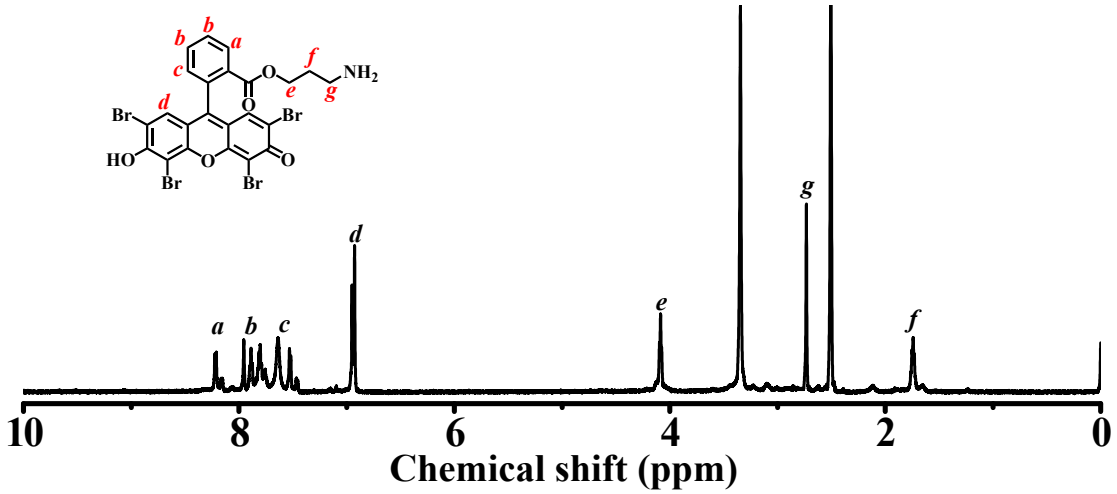

Figure S1. ^{1}H NMR spectrum of EY-NH_2 in DMSO-d_6.

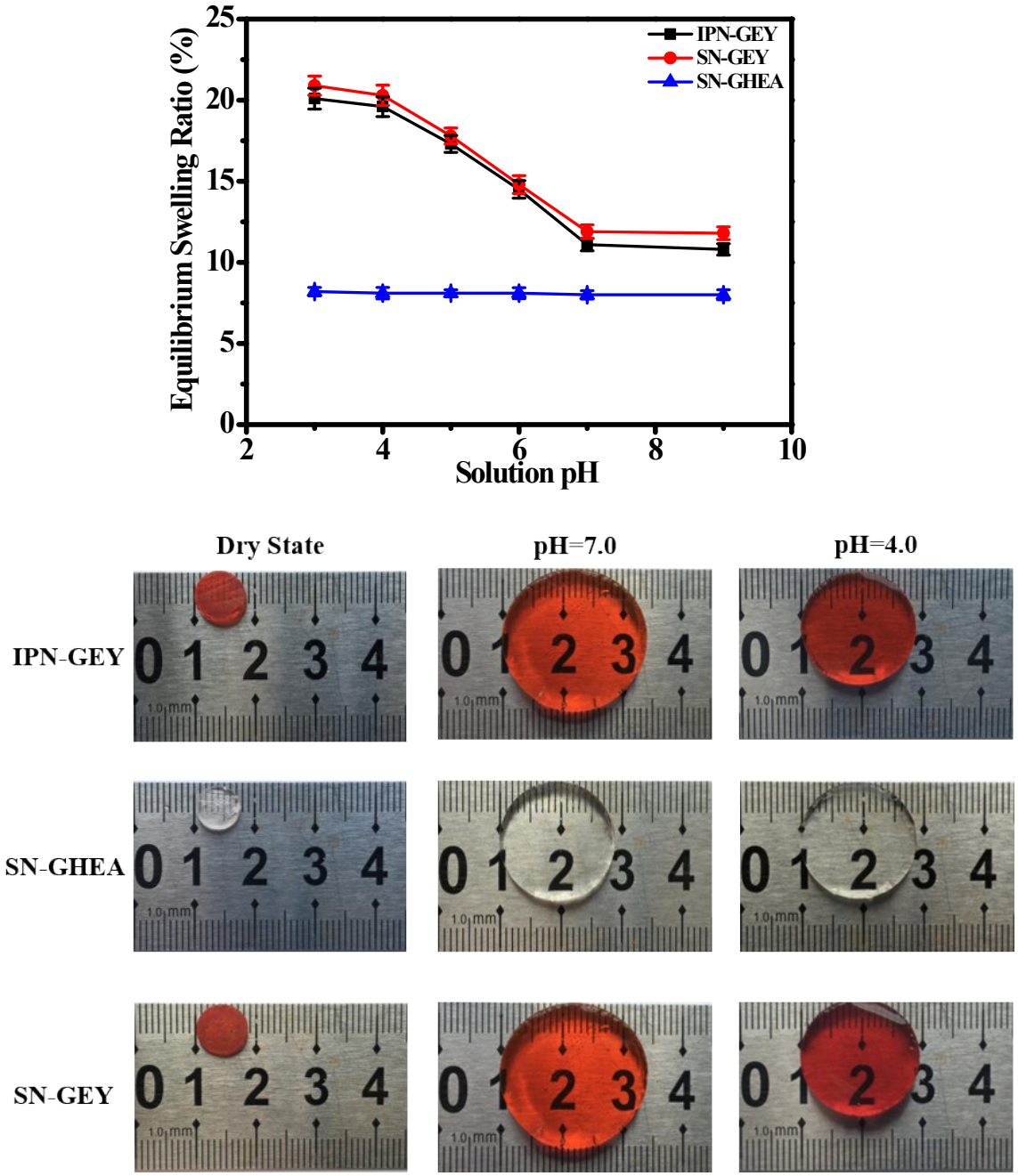

Figure S2. Influence of decreasing solution pH on the equilibrium swelling ratios of the IPN-GEY, SN-GEY and SN-GHEA gels in aqueous media.

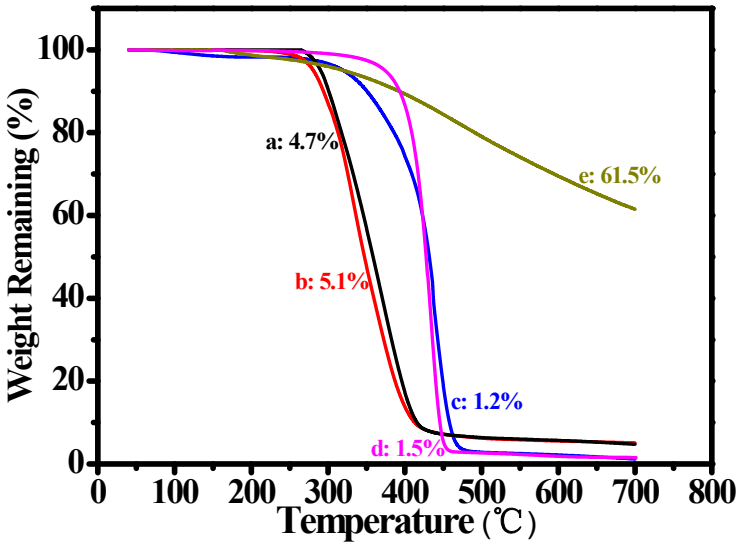

Figure S3. TGA curves of the (a) IPN-GEY, (b) SN-GEY, (c) SN-GHEA, (d) SN-GDEAPA gels and (e) EY-NH_2.

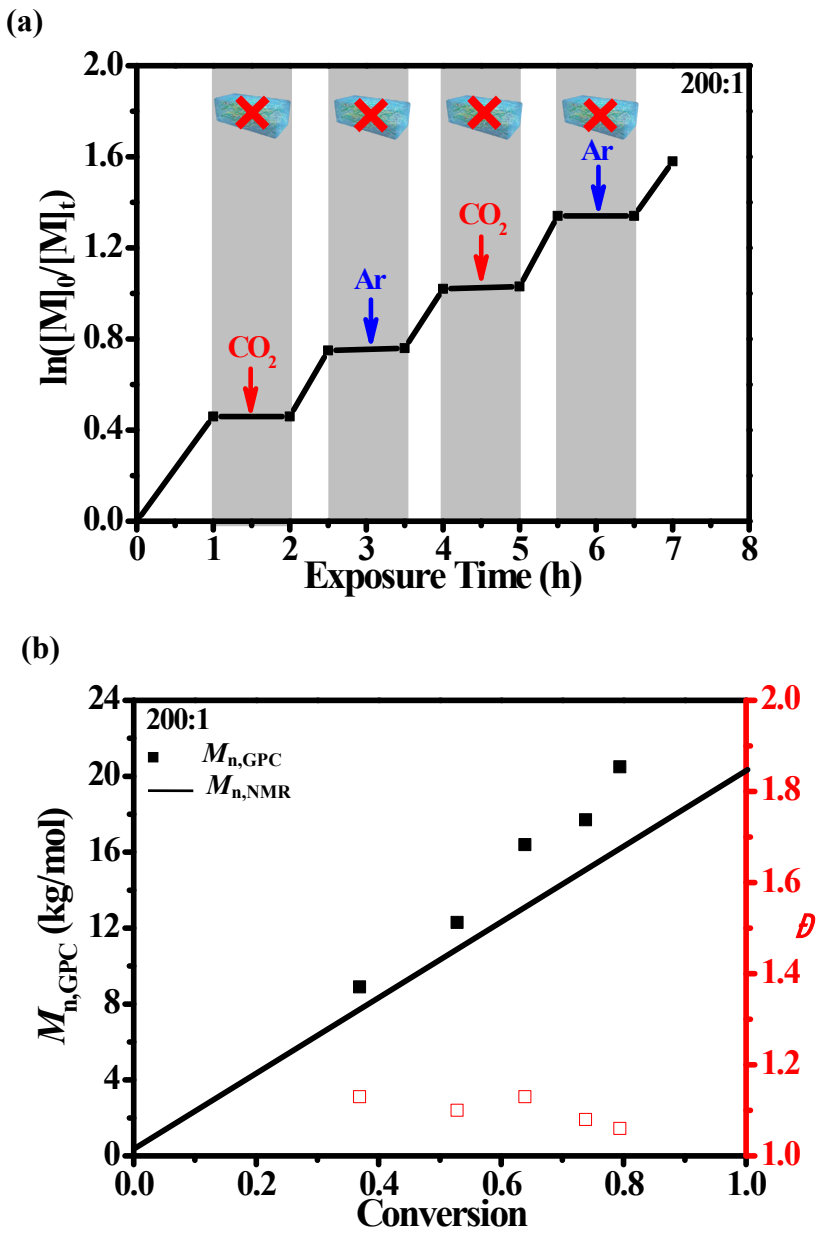

Figure S4. Kinetic analyses of PET-RAFT polymerization of DMA with IPN-GEY gel (2×2×2 mm^3 in dry state) in aqueous media with prior deoxygenation at 25 ℃ under green LED light (4.8 W, λ_{max} = 520 nm, 1.0 mW/cm^2) with BTPA as the CTA; (a) temporal control over polymerization IN/OUT switches of gels and HIGH/LOW switches of solution pH by CO_2/Ar purging and (b) evolution of $M_{n,NMR}$, $M_{n,GPC}$ and $Đ$ versus monomer conversion.

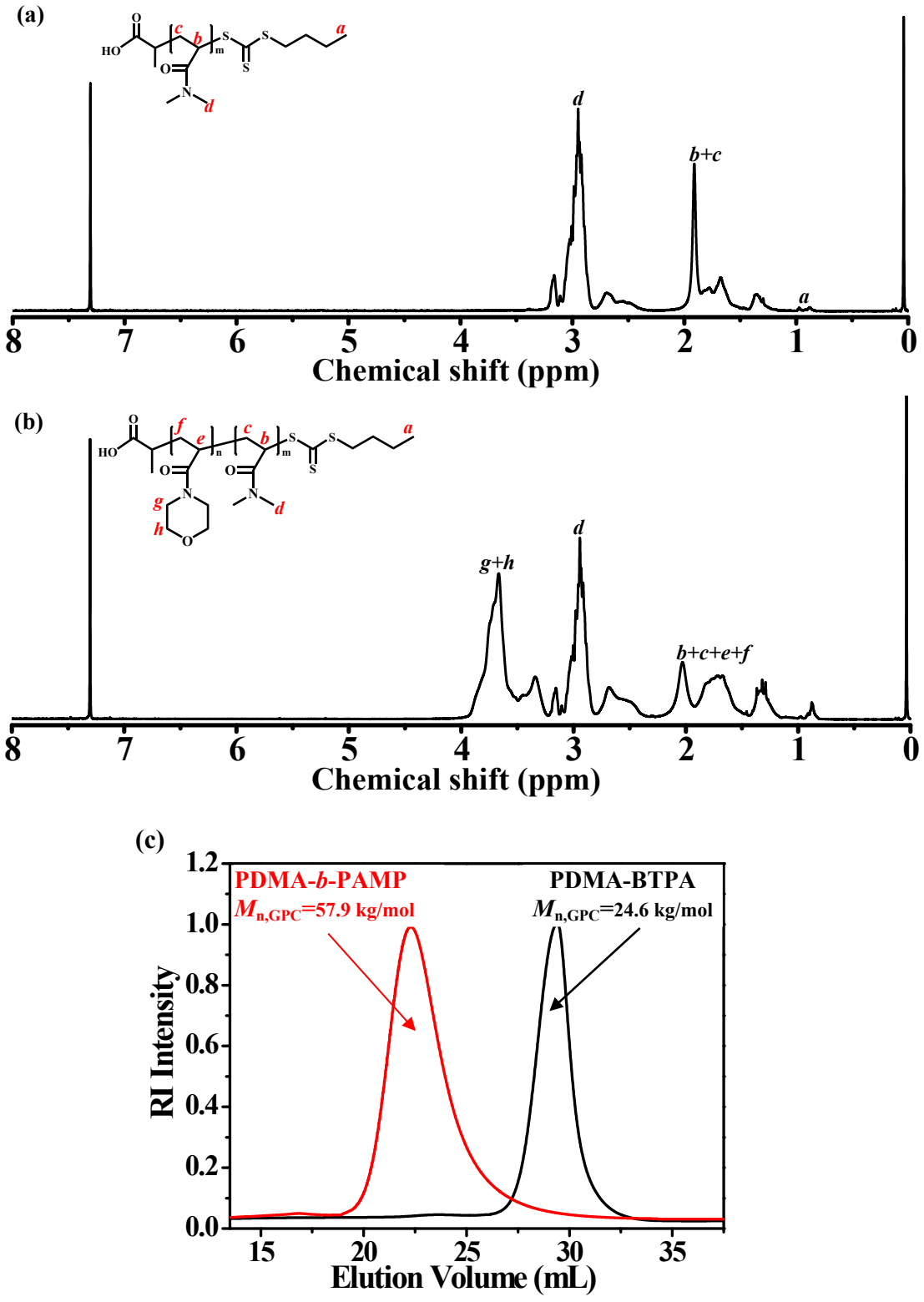

Figure S5. ^{1}H NMR spectra of (a) PDMA-BTPA and (b) PDMA-*b*-PAMP in $CDCl_3$ and (c) GPC profiles for evolution of molecular weight of PDMA-BTPA and PDMA-*b*-PAMP.

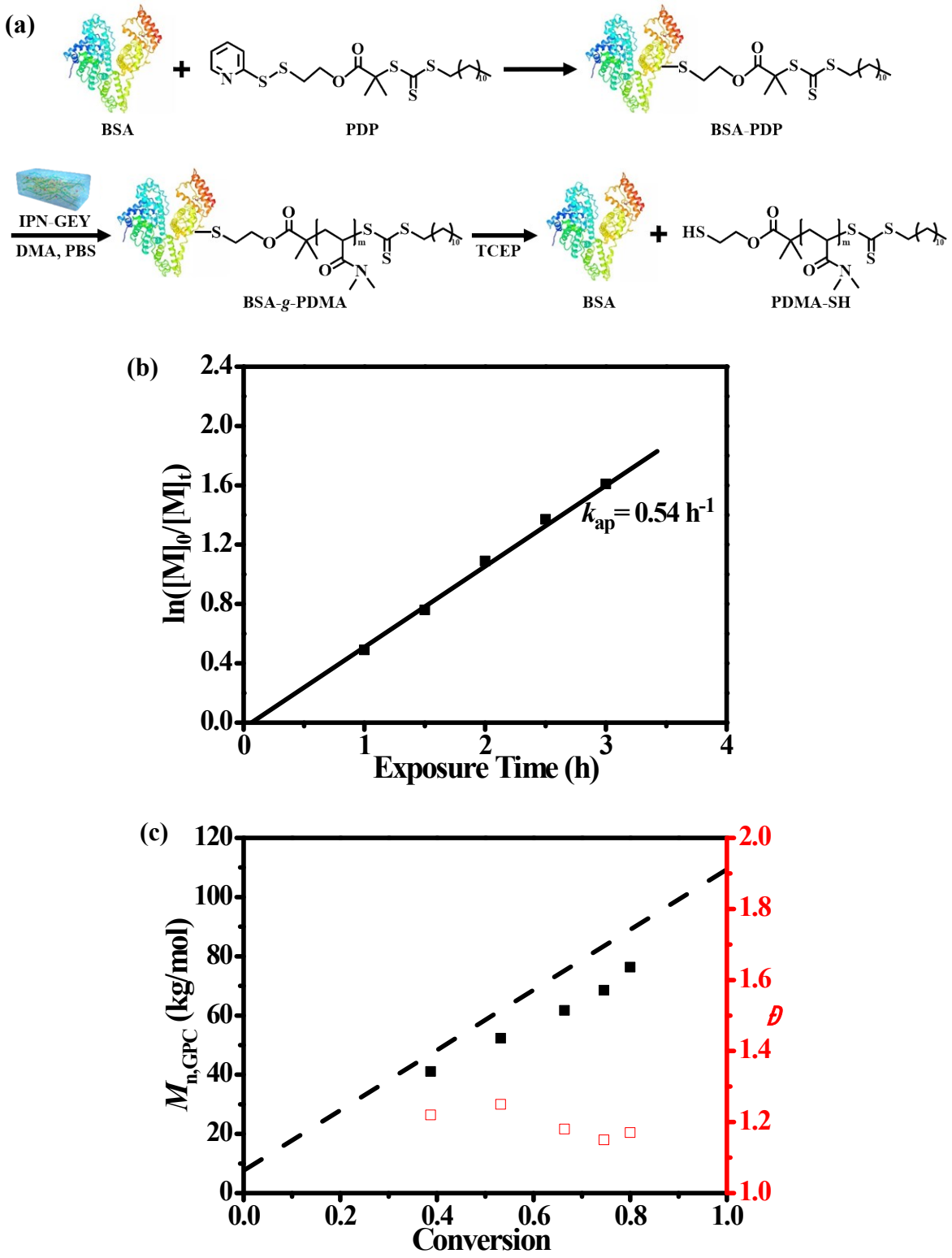

Figure S6. Bioconjugation of BSA-*g*-PDMA by the aqueous PET-RAFT polymerization technique: (a) synthetic route towards BSA-*g*-PDMA bioconjugates, (b) plot of $\ln[M]_0/[M]_t$ versus exposure time t and (c) evolution of $M_{n,th}$, $M_{n,GPC}$ and $Đ$ versus monomer conversion.

Table S1. Synthesis of SN-GHEA, SN-GEY and IPN-GEY Gels

Entry	Gel	1st Network[a]	Feed Ratio	2nd Network	Feed Ratio	[PGE]/[HEA]	Addition Time[b] (h)	Mechanical Property
1	SN-GEY-1	PGE/EY-NH_2/DEAPA/BAE	20:1:7:6	-	-	-	-	Soft, fragile
2	SN-GEY-2	PGE/EY-NH_2/DEAPA/BAE	20:1:5:7	-	-	-	-	Soft, fragile
3	SN-GEY-3	PGE/EY-NH_2/DEAPA/BAE	20:1:3:8	-	-	-	-	Soft, fragile
4	SN-GEY-4	PGE/EY-NH_2/DEAPA/BAE	20:1:2.2:8.4	-	-	-	-	Moderate
5	SN-GEY	PGE/EY-NH_2/DEAPA/BAE	20:1:1:9	-	-	-	-	Moderate
6	SN-GDEAPA	PGE/DEAPA/BAE	20:2:9	-	-	-	-	Moderate
7	SN-GHEA-1	-	-	HEA/TEGDA	100:20	-	-	Hard
8	SN-GHEA-2	-	-	HEA/TEGDA	100:10	-	-	Hard
9	SN-GHEA-3	-	-	HEA/TEGDA	100:8	-	-	Hard
10	SN-GHEA-4	-	-	HEA/TEGDA	100:5	-	-	Soft, fragile
11	SN-GHEA	-	-	HEA/TEGDA	100:6	-	-	Moderate
12	IPN-GEY-1	PGE/EY-NH_2/DEAPA/BAE	20:1:1:9	HEA/TEGDA	100:6	1:1	0	Hard, network separation
13	IPN-GEY-2	PGE/EY-NH_2/DEAPA/BAE	20:1:1:9	HEA/TEGDA	100:6	1:1	4	Hard, network separation
14	IPN-GEY-3	PGE/EY-NH_2/DEAPA/BAE	20:1:1:9	HEA/TEGDA	100:6	1:1	7	Hard
15	IPN-GEY-4	PGE/EY-NH_2/DEAPA/BAE	20:1:1:9	HEA/TEGDA	100:6	3:2	7	Hard
16	IPN-GEY	PGE/EY-NH_2/DEAPA/BAE	20:1:1:9	HEA/TEGDA	100:6	2:1	7	Moderate

[a] Abbreviations: poly(ethylene glycol) diglycidyl ether (PGE), amino-functionalized eosin Y (EY-NH_2), 1,2-bis(2-aminoethoxy)ethane (BAE), 3-(diethylamino)propylamine (DEAPA), 2-hydroxyethyl acrylate (HEA), tetra(ethylene glycol) diacrylate (TEGDA).

[b] Addition time refers to the time interval for feeding the components of 2nd network into the reaction mixture.

Table S2. PET-RAFT Polymerization of Varied Monomers Using IPN-GEY Gels as Photocatalysts

Entry	Photocatalyst	Monomer	CTA	Solvent	[M]/[CTA]	Time (h)	α[b] (%)	$M_{n,NMR}$[b] (kg/mol)	$M_{n,GPC}$[c] (kg/mol)	$Đ$[c]
1[d]	IPN-GEY	DEA	BTPA	water	200	2	56	14.5	18.2	1.12
2	IPN-GEY	DEA	BTPA	water	200	6	88	22.6	31.9	1.08
3	IPN-GEY	NIPAM	BTPA	water	200	6	94	21.5	27.6	1.05
4	IPN-GEY	NIPAM	BTPA	water	400	6	91	41.4	52.3	1.07
5	IPN-GEY	AMP	PEG-DDMAT	water	200	2	63	18.9	27.2	1.14
6	IPN-GEY	AMP	PEG-DDMAT	water	200	6	92	27.0	36.8	1.09
7	IPN-GEY	HEA	PEG-DDMAT	water	200	6	90	22.0	26.7	1.13
8	IPN-GEY	HEA	PEG-DDMAT	water	400	6	86	41.0	55.8	1.15
9	IPN-GEY	PEGMA	BTPA	water	200	12	32	32.2	57.6	1.28
10	IPN-GEY	PEGMA	BTPA	water	200	24	58	58.2	80.5	1.22
11	IPN-GEY	MA	BTPA	DMSO	200	2	65	11.4	14.1	1.08
12	IPN-GEY	MA	BTPA	DMSO	200	6	93	16.2	22.8	1.04
13	IPN-GEY	*t*BA	BTPA	DMSO	200	6	90	23.3	31.6	1.06
14	IPN-GEY	*t*BA	BTPA	DMSO	400	6	86	44.3	58.3	1.09
15	IPN-GEY	GMA	BTPA	DMSO	200	2	68	19.6	28.7	1.08
16	IPN-GEY	GMA	BTPA	DMSO	200	6	96	27.5	38.3	1.05
17	IPN-GEY	PFMA	BTPA	DMSO	200	6	84	40.2	62.5	1.10
18	IPN-GEY	PFMA	BTPA	DMSO	400	6	78	74.5	102.6	1.14
19	IPN-GEY	DMA	BTPA	water	200	12	94	18.9	24.6	1.06
20[e]	IPN-GEY	NIPAM	PDMA-BTPA	water	200	12	96	40.5	49.8	1.07
21[e]	IPN-GEY	AMP	PDMA-BTPA	water	200	12	90	44.2	57.9	1.14
22	IPN-GEY	MA	BTPA	DMSO	200	6	91	15.9	18.4	1.04
23[f]	IPN-GEY	GMA	PMA-BTPA	DMSO	200	6	94	42.6	53.5	1.08
24[f]	IPN-GEY	PFMA	PMA-BTPA	DMSO	200	6	82	54.9	76.1	1.15
25	SN-GHEA	DMA	BTPA	water	200	12	-	-	-	-
26	SN-GDEAPA	DMA	BTPA	water	200	12	-	-	-	-

[a] The polymerizations were performed with IPN-GEY gels (2×2×2 mm^3 in dry state) under green LED light irradiation (4.8 W, λ_{max} = 520 nm, 1.0 mW/cm^2) with prior deoxygenation at 25 ºC.

[b] The molecular weight was calculated using the following equation: $M_{n,NMR} = [M]_0/[CTA] \times M_n(M) \times \alpha + M_n(CTA)$, where $[M]_0$, [CTA], $M_n(M)$, α and $M_n(CTA)$ correspond to initial monomer concentration, initial CTA concentration, molecular weight of monomer, monomer conversion derived from ^{1}H NMR spectroscopy, and molecular weight of CTA.
[c] Derived from GPC profiles (calibration with PMMA molecular weight standards), polydispersity index ($Đ$) = $M_{w,GPC}/M_{n,GPC}$.
[d] Abbreviations: chain transfer agent (CTA), *N,N*-dimethylacrylamide (DMA, 99.1 g/mol), *N,N*-diethylacrylamide (DEA, 127.2 g/mol), *N*-isopropylacrylamide (NIPAM, 113.2 g/mol), 4-acryloylmorpholine (AMP, 141.2 g/mol), 2-hydroxyethyl acrylate (HEA, 116.1 g/mol), poly(ethylene glycol) methyl ether methacrylate (PEGMA, 500 g/mol), methyl acrylate (MA, 86.1 g/mol), *tert*-butyl acrylate (*t*BA, 128.2 g/mol), glycidyl methacrylate (GMA, 142.2 g/mol), pentafluorophenyl methacrylate (PFMA, 238.1 g/mol), 2-(butyltrithiocarbonothioylthio)propionic acid (BTPA, 238 g/mol), methoxy poly(ethylene glycol) 2-(dodecylthiocarbonothioylthio)-2-methylpropionate (PEG-DDMAT, 1100 g/mol).
[e] The block copolymers were synthesized using PDMA-BTPA in Entry 19 as macro-CTA.
[f] The block copolymers were synthesized using PMA-BTPA in Entry 22 as macro-CTA.

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