Electronic Supplementary Material (ESI) for Polymer Chemistry.

In Situ Cross-linking Polymerization-Induced Self-Assembly: Not Only Generates Cross-linked Structures But Also Promotes Morphology Transition by the Cross-linker

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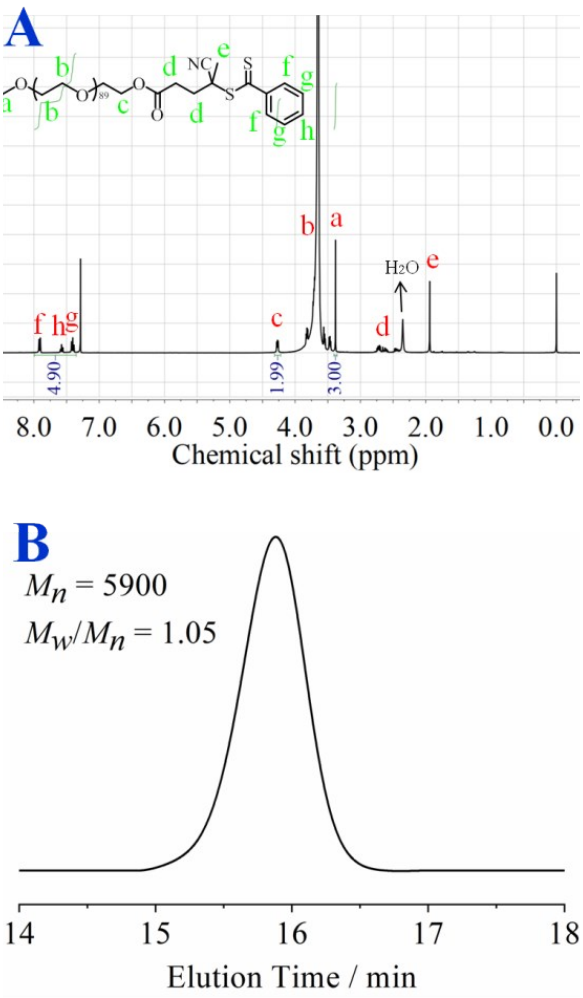

Fig. S1 (A) ^{1}H NMR spectrum and (B) GPC curve of PEG_{90}-CPADB macro RAFT agent.

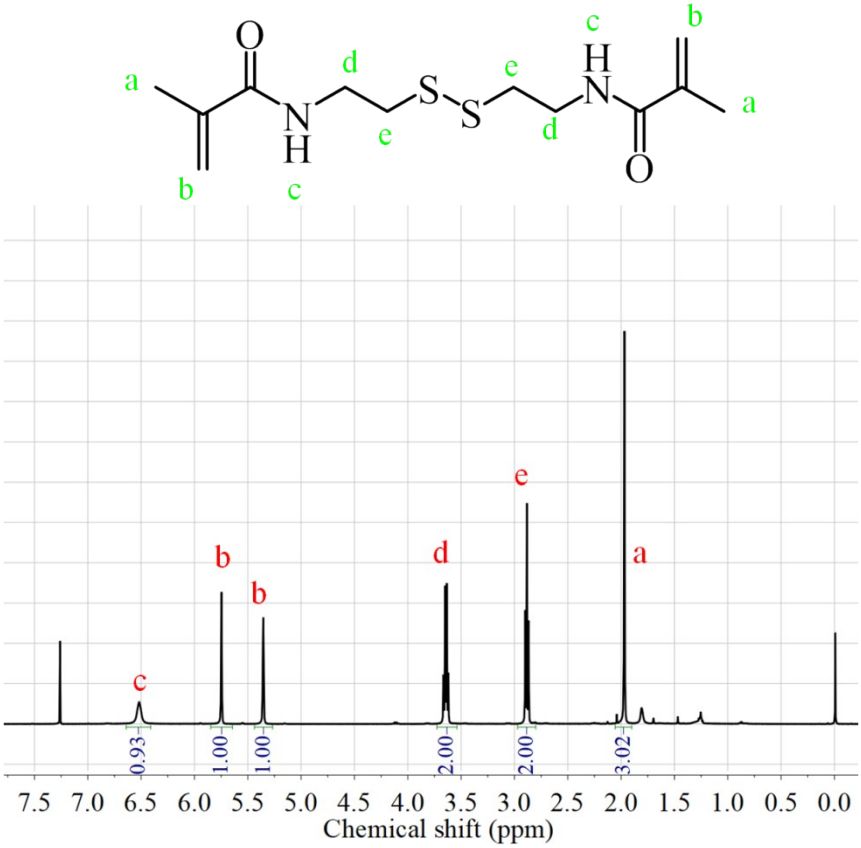

Fig. S2 ^{1}H NMR spectrum of the cross-linker cystaminebismethacrylamide (CBMA) in $CDCl_3$.

Table S1. Summary of results obtained by PEG_{90}-CPADB mediated RAFT dispersion copolymerization of DIPEMA and CBMA (DIPEMA/PEG_{90}-CPADB = 150, CBMA/DIPEMA = 5%) at different polymerization time, monomer conversion, M_n and M_w/M_n of the resultant polymers.

Polymerization time	[a]Conversion of DIPEMA (%)	[a]Conversion of CBMA (%)	[a]Statistical DIPEMA units	[a]Statistical CBMA units	[b]$M_{n,GPC}$ (kg/mol)	[b]M_w/M_n
0.5 h	8.6	3.8	12.8	0.28	14.2	1.06
1 h	16.7	7.6	25.1	0.57	17.9	1.18
2 h	46.8	15.1	70.3	1.13	28.7	1.41
3 h	54.4	20.8	81.6	1.56	--	--
4 h	72.7	26.4	109.1	1.98	--	--
6 h	85.7	34.0	128.6	2.55	--	--
9 h	90.2	54.7	135.3	4.10	--	--
12 h	91.0	62.3	136.6	4.67	--	--
24 h	92.5	71.7	138.7	5.38	--	--

[a]The conversion of DIPEMA and CBMA, the statistical DIPEMA units and CBMA units in the resultant PEG_{90}-*b*-P($DIPEMA_x$-*co*-$CBMA_y$) were calculated according to the ^1H NMR spectra of the reaction media as shown in Figure S3. [b]The M_n and M_w/M_n of the resultant PEG_{90}-*b*-P($DIPEMA_x$-*co*-$CBMA_y$) were determined by GPC.

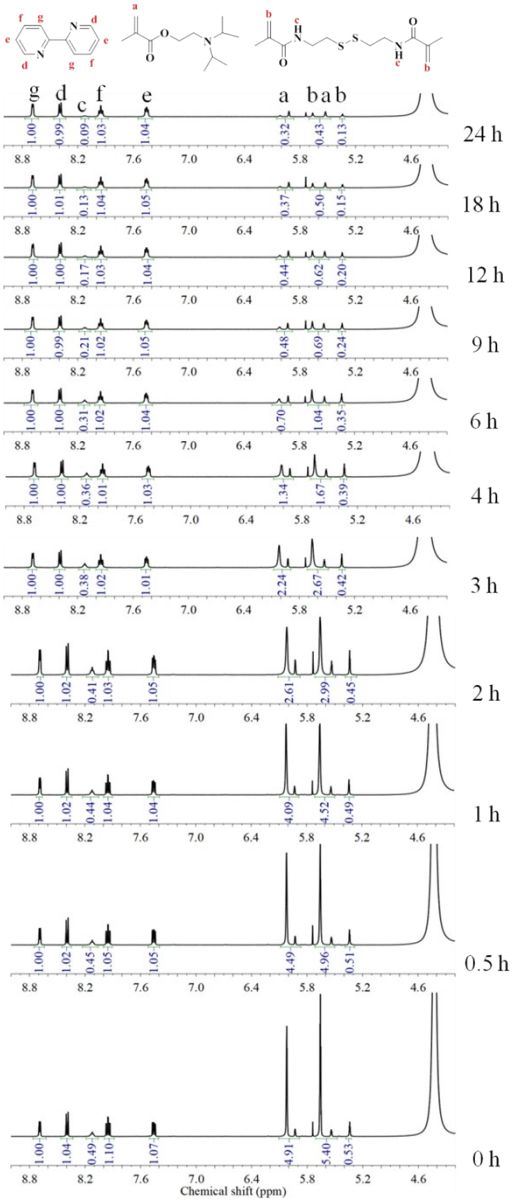

Fig. S3 ^{1}H NMR spectra of the reaction mixture of PEG_{90}-CPADB-mediated RAFT dispersion copolymerization of DIPEMA and CBMA (DIPEMA/PEG_{90}-CPADB = 150, CBMA/DIPEMA = 5%) at different polymerization times. 2,2'-Bipyridine was used as an internal standard to calculate the conversion of the monomer (DIPEMA) and cross-linker (CBMA). 50 μL of the reaction mixture was taken out for ^{1}H-NMR (DMSO-d_6) at specific time of polymerization. The calculation formula is as follows:

Conversion $(\%)_{DIPEMA} = (1 - a_t/a_0) \times 100\%$

Conversion $(\%)_{CBMA} = (1 - b_t/b_0) \times 100\%$

The integral values of vinyl protons of DIPEMA (a) and CBMA (b) at 0 h of polymerization are denoted as a_0 and b_0, respectively. The integral values of vinyl protons of DIPEMA (a) and CBMA (b) at t h of polymerization are denoted as a_t and b_t, respectively. ***PS*:** In order to simplify the calculation, we assumed that the peak b was only contributed by the unreacted CBMA monomer in the solution and ignored the contribution of the CBMA units that were not completely reacted in the polymer. The peaks at 5.73 ppm were due to residual dichloromethane in the NMR tubes (The NMR tubes were washed with dichloromethane).

Table S2. Summary of results obtained by PEG_{90}-CPADB mediated RAFT dispersion polymerization of DIPEMA at different polymerization time, monomer conversion, M_n and M_w/M_n of the resultant polymers.

Polymerization time	[a]Conversion of DIPEMA (%)	[a]$DP_{PDIPEMA}$	[b]$M_{n,NMR}$ (kg/mol)	[c]$M_{n,GPC}$ (kg/mol)	[c]M_w/M_n
1 h	14.7	22	10.3	13.4	1.14
2 h	35.2	53	17.0	15.3	1.11
3 h	52.5	79	22.6	19.7	1.09
4 h	62.2	93	24.2	23.1	1.08
6 h	81.1	122	29.6	28.7	1.15
9 h	91.4	137	30.9	31.1	1.16
12 h	92.2	138	31.8	32.2	1.17
24 h	92.4	139	32.5	32.6	1.17

[a]The conversion of DIPEMA and $DP_{PDIPEMA}$ were calculated according to the ^{1}H NMR spectra of the reaction media as shown in Fig. S2. [b]$M_{n,NMR}$ of the block copolymer PEG_{90}-*b*-$PDIPEMA_x$ were calculated based on the ^{1}H NMR spectra as shown in Fig. S4. [c]The M_n and M_w/M_n of the block copolymer PEG_{90}-*b*-$PDIPEMA_x$ were determined by GPC.

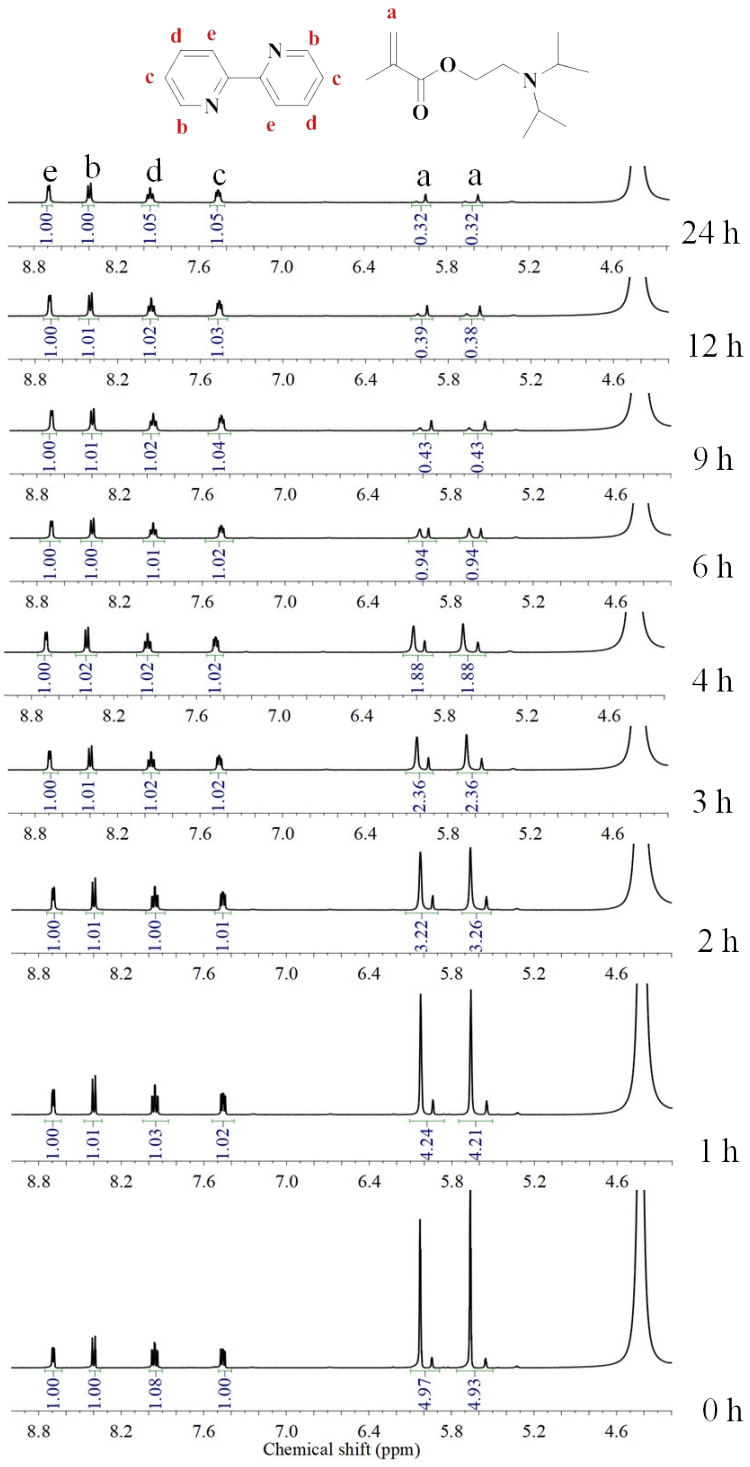

Fig. S4 ^{1}H NMR spectra of the reaction mixture (RAFT dispersion polymerization of DIPEMA targeted to PEG_{90}-*b*-$PDIPEMA_{150}$) at different polymerization times. 2,2'-Bipyridine was used as an internal standard to calculate the conversion of the monomer (DIPEMA). 50 µL of the reaction mixture was taken out for ^{1}H NMR (DMSO-d_6) at specific time of polymerization. The calculation formula is as follows:

Conversion $(\%)_{DIPEMA} = (1 - a_t/a_0) \times 100\%$

The integral value of vinyl protons of DIPEMA (a) at 0 h and t h of polymerization is denoted as a_0 and a_t, respectively.

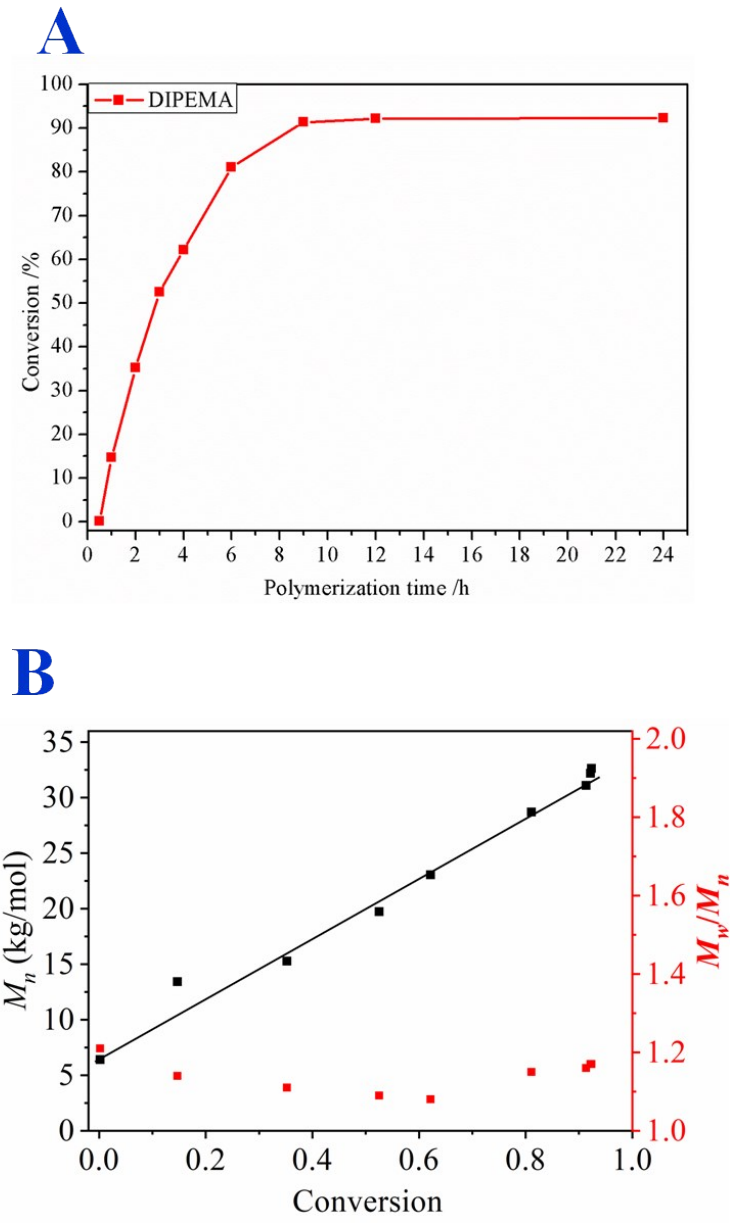

Fig. S5 (A) Monomer conversion at different polymerization time of the PEG_{90}-CPADB-mediated RAFT dispersion polymerization of DIPEMA (DIPEMA/PEG_{90}-CPADB = 150). (B) Evolution of M_n and M_w/M_n with monomer conversion for the PEG_{90}-CPADB-mediated RAFT dispersion polymerization of DIPEMA (DIPEMA/PEG_{90}-CPADB = 150).

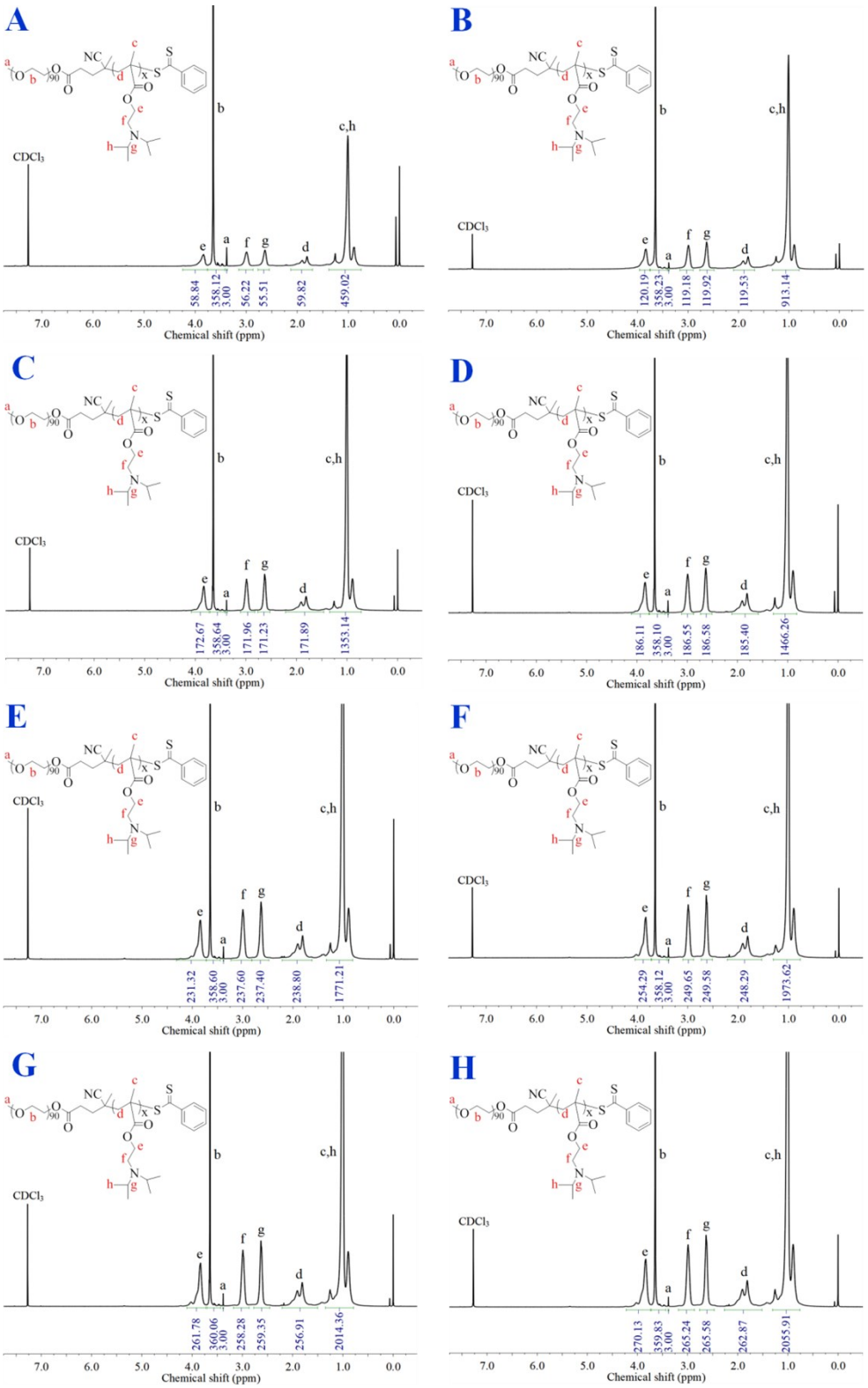

Fig. S6 ^{1}H NMR spectra of the block copolymer PEG_{90}-*b*-$PDIPEMA_x$ obtained by RAFT dispersion polymerization of DIPMEA (targeted $DP_{PDIPEMA}$ = 150) at different polymerization time, (A) 1 h, (B) 2 h, (C) 3 h, (D) 4 h, (E) 6 h, (F) 9 h, (G) 12 h and (H) 24 h.

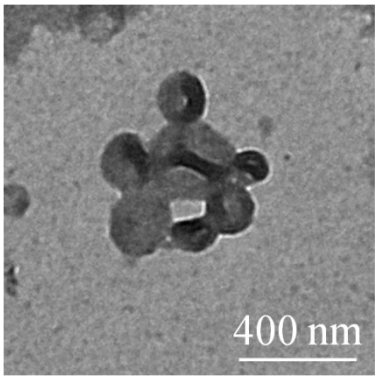

Fig. S7 TEM images of the PEG_{90}-*b*-P($DIPEMA_{140}$-*co*-$CBMA_{5.66}$) vesicles (as shown in Fig. $3F_2$) after the processing of THF, (1) the vesicles were dispersed in THF, (2) the dispersions in THF were diluted with ethanol/water (7/3) to a specific concentration (0.5 wt%) for TEM characterization.

Table S3. Summary of results obtained by PEG_{90}-CPADB mediated RAFT dispersion copolymerization of DIPEMA and CBMA (DIPEMA/PEG_{90}-CPADB = 150, CBMA/DIPEMA = 10%) at different polymerization time, monomer conversion, M_n and M_w/M_n of the resultant polymers.

Polymerization time	[a]Conversion of DIPEMA (%)	[a]Conversion of CBMA (%)	[a]Statistical DIPEMA units	[a]Statistical CBMA units	[b]$M_{n,GPC}$ (kg/mol)	[b]M_w/M_n
1 h	14.9	5.9	22.4	0.89	21.8	1.35
2 h	39.7	12.9	59.6	1.93	--	--
3 h	48.3	18.8	72.5	2.82	--	--
4 h	64.3	22.8	96.5	3.42	--	--
6 h	78.3	31.7	117.5	4.75	--	--
9 h	85.3	54.5	128.0	8.17	--	--
12 h	89.2	65.4	133.7	9.80	--	--
24 h	90.1	75.3	135.1	11.29	--	--

[a]The conversion of DIPEMA and CBMA, the statistical DIPEMA units and CBMA units in the resultant PEG_{90}-*b*-P($DIPEMA_x$-*co*-$CBMA_y$) were calculated according to the ^1H NMR spectra of the reaction media as shown in Fig. S8. [b]The M_n and M_w/M_n of the resultant PEG_{90}-*b*-P($DIPEMA_x$-*co*-$CBMA_y$) were determined by GPC.

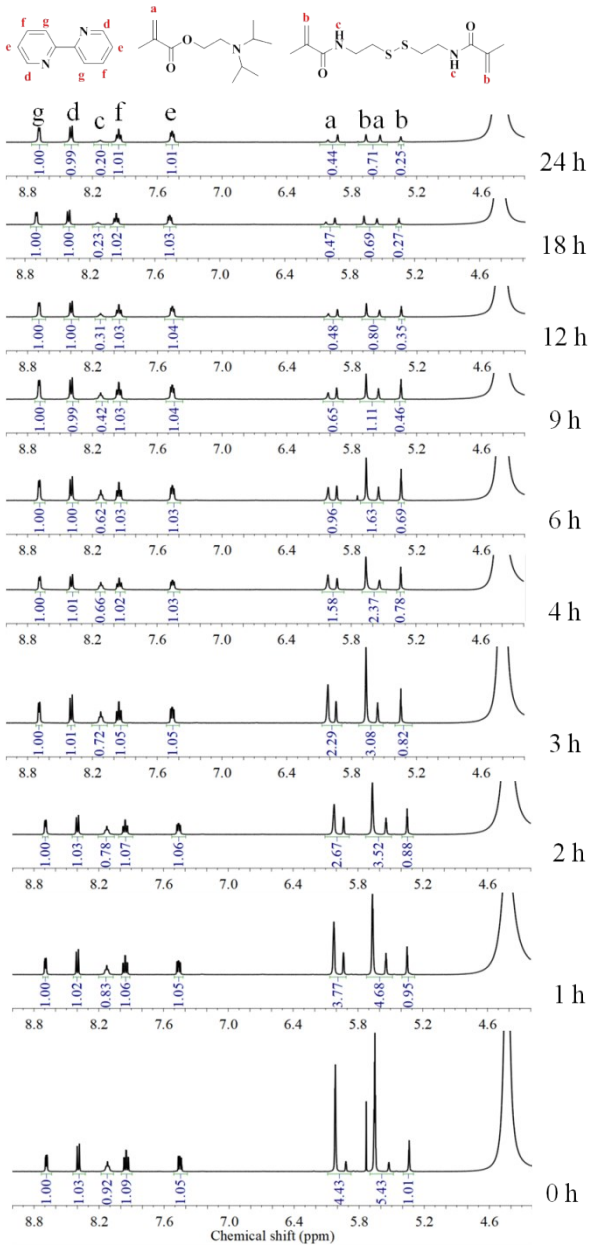

Fig. S8 ^{1}H-NMR spectra of the reaction mixture of PEG_{90}-CPADB-mediated RAFT dispersion copolymerization of DIPEMA and CBMA (DIPEMA/PEG_{90}-CPADB = 150, CBMA/DIPEMA = 10%) at different polymerization times. 2,2'-Bipyridine was used as an internal standard to calculate the conversion of the monomer (DIPEMA) and cross-linker (CBMA). 50 µL of the reaction mixture was taken out for ^{1}H-NMR (DMSO-d_6) at specific time of polymerization. The calculation formula is as follows:

Conversion $(\%)_{DIPEMA} = (1 - a_t/a_0) \times 100\%$

Conversion $(\%)_{CBMA} = (1 - b_t/b_0) \times 100\%$

The integral values of vinyl protons of DIPEMA (a) and CBMA (b) at 0 h of polymerization are denoted as a_0 and b_0, respectively. The integral values of vinyl protons of DIPEMA (a) and CBMA (b) at t h of polymerization are denoted as a_t and b_t, respectively. ***PS*:** In order to simplify the calculation, we assumed that the peak b was only contributed by the unreacted CBMA monomer in the solution and ignored the contribution of the CBMA units that were not completely reacted in the polymer. The peaks at 5.73 ppm were due to residual dichloromethane in the NMR tubes (The NMR tubes were washed with dichloromethane).

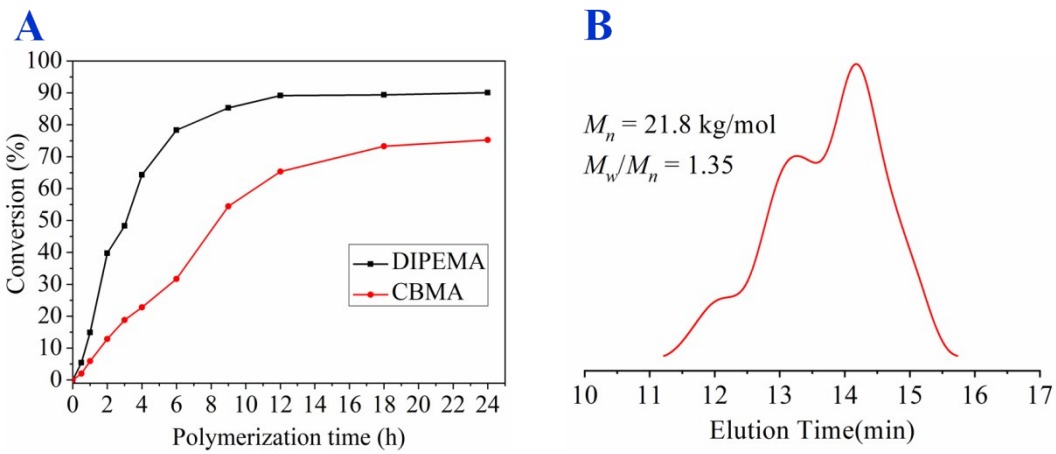

Fig. S9 (A) Conversion of DIPEMA (black line) and CBMA (red line) at different polymerization time of the PEG_{90}-CPADB-mediated RAFT dispersion copolymerization of DIPEMA and CBMA (DIPEMA/PEG_{90}-CPADB = 150, CBMA/DIPEMA = 10%). (B) GPC traces of the PEG_{90}-*b*-P(DIPEMA-*co*-CBMA) block copolymers obtained at 1 h of polymerization for the PEG_{90}-CPADB-mediated RAFT dispersion copolymerization of DIPEMA and CBMA (DIPEMA/PEG_{90}-CPADB = 150, CBMA/DIPEMA = 10%). The GPC characterization for the PEG_{90}-*b*-P($DIPEMA_x$-*co*-$CBMA_y$) formed after 2 h of polymerization is not conducted due to the cross-linked (or partially cross-linked) structures.

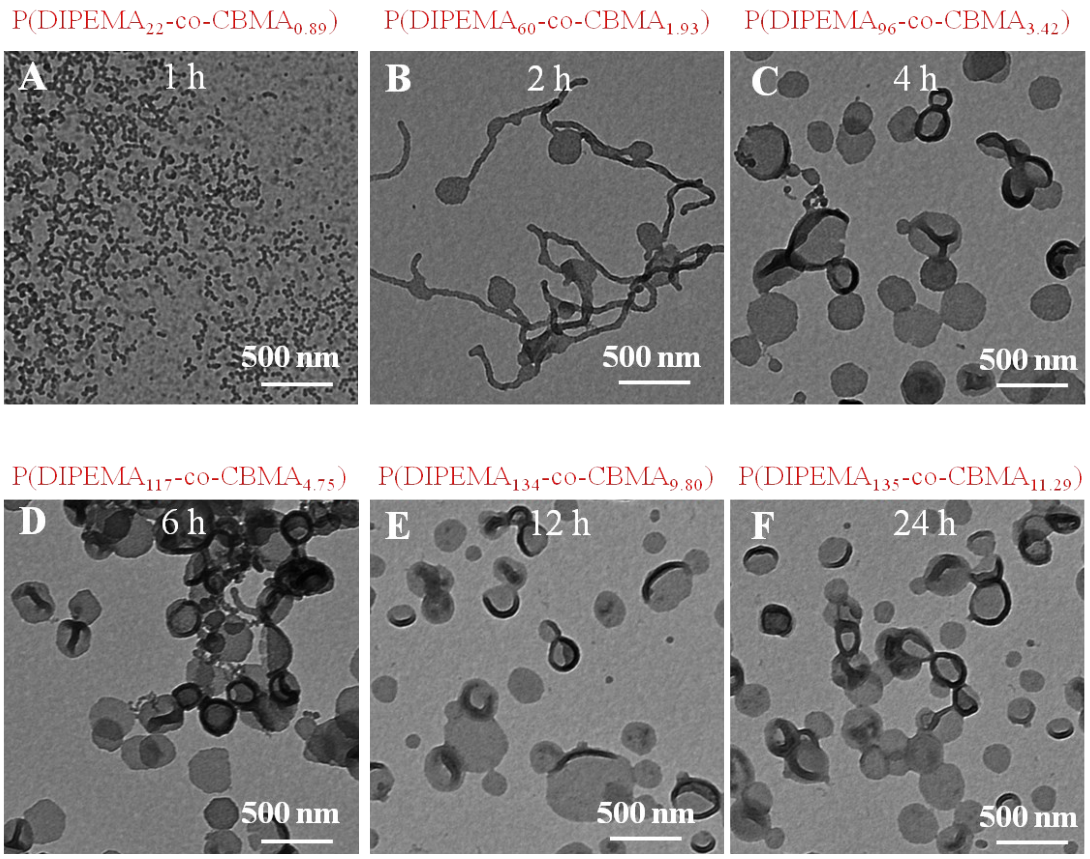

Fig. S10 TEM images (A-F) of the PEG_{90}-P($DIPEMA_x$-*co*-$CBMA_y$) nano-objects obtained at different polymerization time by PEG_{90}-CPADB mediated RAFT dispersion copolymerization of DIPEMA and CBMA (DIPEMA/PEG_{90}-CPADB = 150, CBMA/DIPEMA = 10%). The red note on the top of each image is the composition of the solvophobic blocks in corresponding nano-objects. The subscript number of DIPEMA and CBMA is the statistical units of DIPEMA and CBMA in the formed P(DIPEMA-*co*-CBMA) blocks, respectively, which is calculated according to the ^{1}H NMR spectra as shown in Fig. S8.

Table S4. Summary of results obtained by RAFT dispersion polymerization of DIPEMA and CBMA, monomer conversion, M_n and M_w/M_n of the resultant polymers, morphology of the resultant nano-objects.

[a]Samples	[b]Conversion of DIPEMA (%)	[b]Conversion of CBMA (%)	[c]M_n (g/mol)	[c]M_w/M_n	[d]Morphology
$D_{60}C_0$	93.3	-	18800	1.20	S
$D_{80}C_0$	91.3	-	21900	1.23	S
$D_{100}C_0$	92.0	-	26100	1.26	S+W
$D_{120}C_0$	92.5	-	29400	1.15	S+W
$D_{150}C_0$	90.7	-	32300	1.19	L+V
$D_{60}C_{5\%}$	93.8	78.3	-	-	S+W
$D_{80}C_{5\%}$	93.0	76.9	-	-	S+W+L
$D_{100}C_{5\%}$	92.5	72.0	-	-	L
$D_{120}C_{5\%}$	91.2	72.5	-	-	V
$D_{150}C_{5\%}$	90.0	67.0	-	-	V
$D_{60}C_{10\%}$	93.0	78.3	-	-	W
$D_{80}C_{10\%}$	92.4	80.6	-	-	W
$D_{100}C_{10\%}$	92.0	80.0	-	-	W
$D_{120}C_{10\%}$	91.4	77.1	-	-	W+L
$D_{150}C_{10\%}$	90.5	76.0	-	-	L+V

[a]brief notation of each sample, wherein D represents PDIPEMA, the subscript number of D is the target $DP_{PDIPEMA}$, C represents CBMA, the subscript number of C is the feed molar ratio of CBMA/DIPEMA. [b]The monomer conversion was calculated according to the ^{1}H NMR spectra of the reaction media. [c]The M_n and M_w/M_n were determined by GPC. [d]The morphology of each sample was identified by TEM, wherein S represents spherical micelles, W denotes worms, L is lamella, and V represents vesicles.

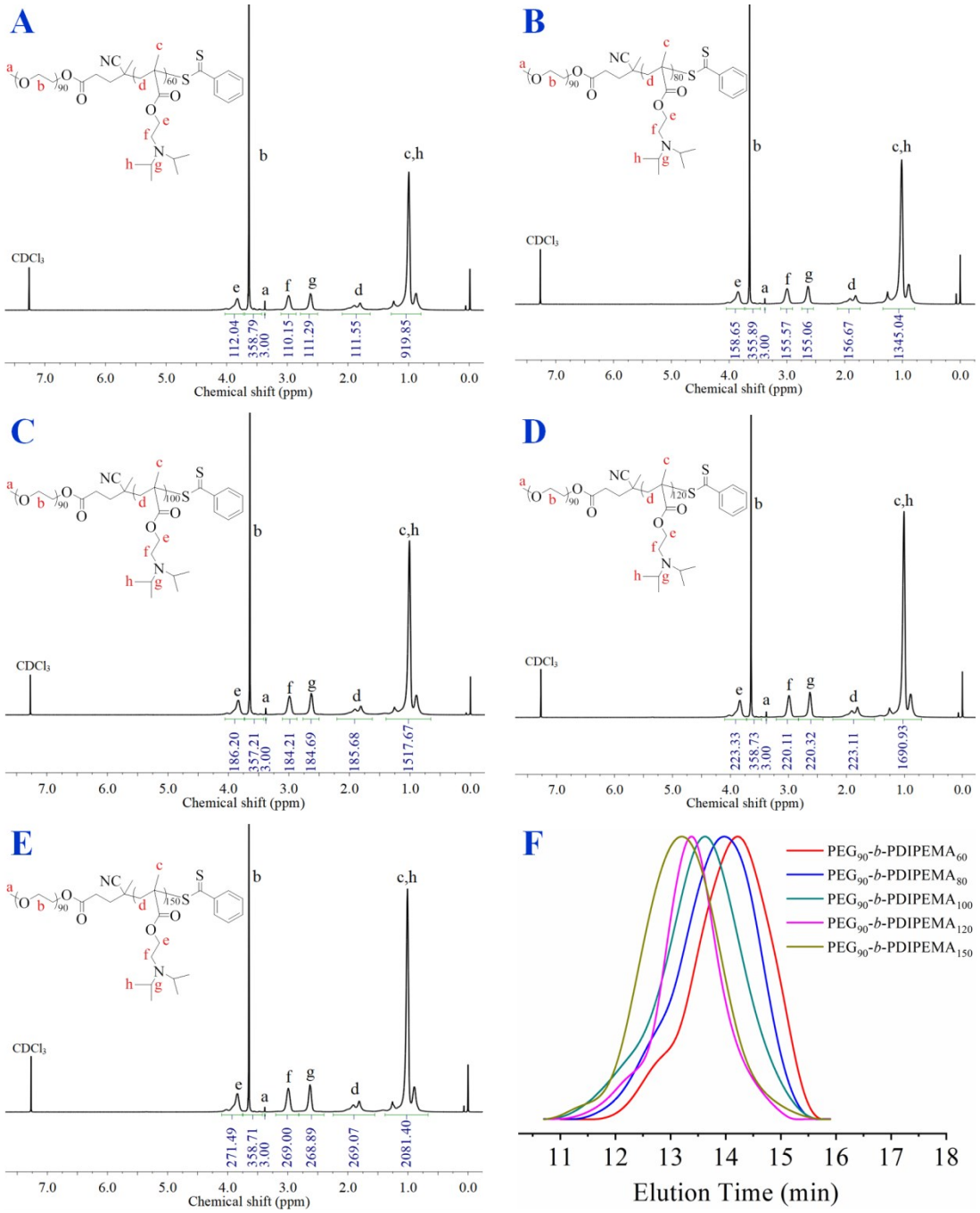

Fig. S11 ^{1}H NMR spectra of the block copolymers (A) PEG_{90}-*b*-$PDIPEMA_{60}$, (B) PEG_{90}-*b*-$PDIPEMA_{80}$, (C) PEG_{90}-*b*-$PDIPEMA_{100}$, (D) PEG_{90}-*b*-$PDIPEMA_{120}$, and (E) PEG_{90}-*b*-$PDIPEMA_{150}$ obtained by RAFT dispersion polymerization of DIPMEA with varying DIPEMA/PEG_{90}-CPADB (60~150). All the polymerizations were carried out for 24 h to make sure high monomer conversion. (F) GPC traces of the block copolymers PEG_{90}-*b*-$PDIPEMA_{60\sim150}$ obtained by RAFT dispersion polymerization of DIPMEA with varying DIPEMA/PEG_{90}-CPADB (60~150) for 24 h.

Table S5. Volume-averaged diameter of the nano-objects at different conditions

[a]Sample	pH 7.4	pH 5.0	pH 7.4 GSH 10mM	pH 5.0 GSH 10mM
$D_{60}C_{5\%}$	123.8±5.3 nm	183.8±3.2 nm	47.8±7.3 nm	8.6±2.4 nm
$D_{80}C_{5\%}$	120.0±2.4 nm	204.9±7.3 nm	53.4±9.0 nm	9.2±1.6 nm
$D_{120}C_{5\%}$	196.8±71.5 nm	290.8±49.9 nm	77.7±34.0 nm	8.5±0.8 nm
$D_{150}C_{5\%}$	304.0±14.6 nm	492.7±97.7 nm	266.5±69.0 nm	9.0±1.7 nm

[a]brief notation of each sample, wherein D represents PDIPEMA, the subscript number of D is the target $DP_{PDIPEMA}$, C represents CBMA, the subscript number of C is the feed molar ratio of CBMA/DIPEMA.

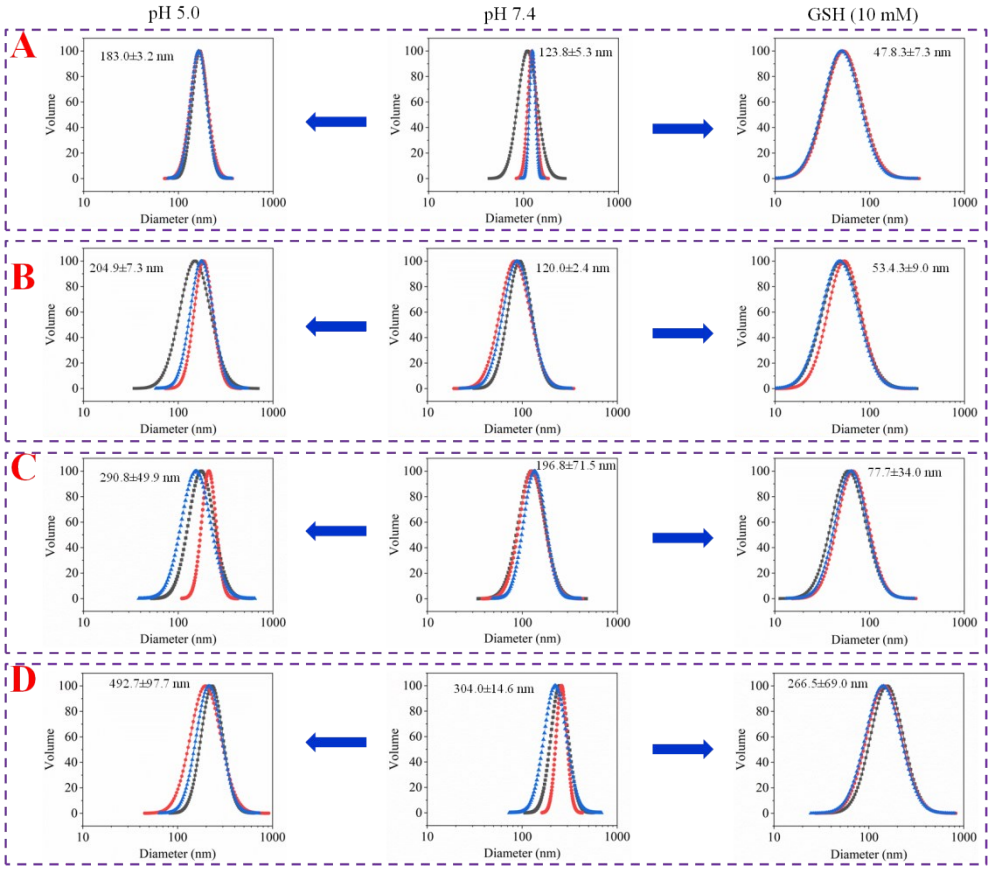

Fig. S12 DLS curves of the nano-objects (A) PEG_{90}-*b*-P($DIPEMA_{60}$-*co*-$CBMA_{5\%}$), (B) PEG_{90}-*b*-P($DIPEMA_{80}$-*co*-$CBMA_{5\%}$), (C) PEG_{90}-*b*-P($DIPEMA_{120}$-*co*-$CBMA_{5\%}$) and (D) PEG_{90}-*b*-P($DIPEMA_{150}$-*co*-$CBMA_{5\%}$) at different conditions.

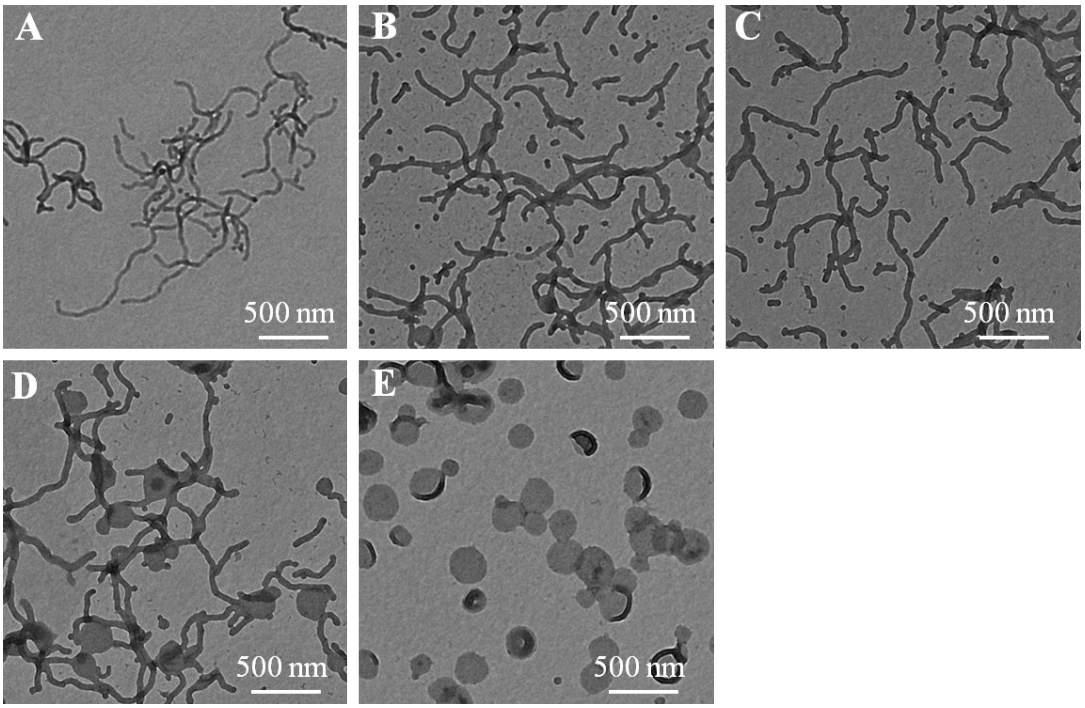

Fig. S13 TEM images of the PEG_{90}-*b*-P($DIPEMA_x$-*co*-$CBMA_{10\%}$) nano-objects obtained by PEG_{90}-CPADB mediated RAFT dispersion copolymerization of DIPEMA and CBMA (CBMA/DIPEMA = 10%) with varying feed molar ratio of DIPEMA/PEG_{90}-CPADB, (A) 60, (B) 80, (C) 100, (D) 120 and (E) 150.

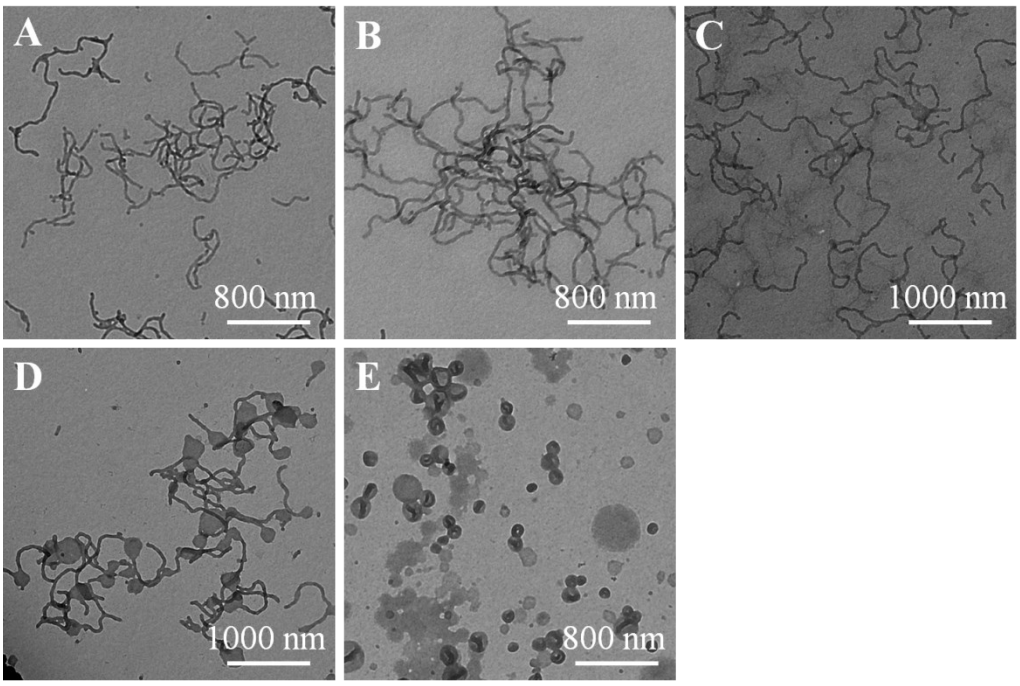

Fig. S14 TEM images of the PEG_{90}-*b*-P($DIPEMA_x$-*co*-$CBMA_y$) nano-objects obtained by PEG_{90}-CPADB mediated RAFT dispersion copolymerization of DIPEMA and CBMA (CBMA/DIPEMA = 10 %) with varying feed molar ratio of DIPEMA/PEG_{90}-CPADB, (A) 60, (B) 80, (C) 100, (D) 120 and (E) 150. All the nano-objects were processed with the following steps: (1) the nano-objects were dispersed in THF, (2) the dispersions in THF were diluted with ethanol/water (7/3) to a specific concentration (0.1 wt%-0.5 wt%) for TEM characterization.