Electronic Supplementary Information

Systematic study on the effects of the structure of block copolymers of PEG and poly(ε-caprolactone-co-glycolic acid) on their temperature-responsive sol-to-gel transition behavior

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MATERIALS AND METHODS

Materials

Poly(ethylene glycol) (PEG) (molecular weight (MW) = 1000 g/mol (PEG_{1000}), 1540 g/mol (PEG_{1540}), and 2000 g/mol (PEG_{2000})), ε-caprolactone (CL), tin-2-ethylhexanoate ($Sn(Oct)_2$), butyric acid anhydride, 4-dimethylaminopyridine (DMAP), anhydrous dichloromethane, as well as other chemicals and organic solvents were purchased from FUJIFILM Wako Pure Chemical Ind., Ltd. (Osaka, Japan). Mono-methoxy poly(ethylene glycol) (MeO-PEG) (MW = 550 g/mol, MeO-PEG_{550}) and glycolide (GL) were obtained from Sigma-Aldrich Co. LLC (St. Louis, MO, USA). Hexamethylene diisocyanate (HMDI) and acetic anhydride (Ac_2O) were purchased from Tokyo Chemical Industry Co. Ltd. (Tokyo, Japan). Branched PEG with four arms (MW = 5000 g/mol, 4-arm PEG_{5000}) was supplied by NOF Co. (Tokyo, Japan). Water was purified using Millipore Elix UV3 direct-Q UV (Merck, Darmstadt, Germany).

Measurements

^{1}H nuclear magnetic resonance (^{1}H-NMR) spectra were obtained through an NMR spectrometer (400 MHz, JNM-GSX-400, JEOL, Tokyo, Japan) using deuterated solvent ($CDCl_3$). The chemical shifts were calibrated using tetramethylsilane (TMS). The number average molecular weight (M_n) of the polymers was calculated from ^{1}H-NMR spectra. The weight average molecular weight (M_w) and polydispersity index (M_w/M_n) of the polymers were determined using size exclusion chromatography (SEC) (column: TSKgel Multipore H_{XL}-M × 2; detector: RI). The measurements were performed using dimethylformamide (DMF) as an eluent with a flow rate of 1.0 mL min^{-1} at 40 °C using a series of PEGs as standards. Temperature-dependent rheological measurements of the sol-to-gel transition of the polymer solutions were performed using a dynamic rheometer (Thermo HAAKE RS600, Thermo Fisher Scientific, Waltham, MA, USA) according to a study reported previously.[1] Thermal analysis of the copolymers and solutions was conducted using a differential scanning calorimeter (DSC-60, Shimadzu) with sealed aluminum pans.

Synthesis of PCGA-PEG-PCGA (ABA triblock copolymer)

ABA triblock copolymers of poly(ε-caprolactone-*co*-glycolide) (PCGA) and PEG (PCGA-PEG-PCGA) were synthesized by ring-opening copolymerization of CL and GL in the presence of PEG as a macroinitiator and $Sn(Oct)_2$ as a catalyst, according to the method described in previous works (**Scheme S1**). [1-3] PEG_{1540} (16.0 g, 10.4 mmol) was dried under *in vacuo* at 120 ºC for 5 h in a 100-mL flask with a stopcock. After cooling to room temperature (r.t.), CL (34.4 g, 302 mmol), GL (6.04 g, 52.1 mmol), and $Sn(Oct)_2$ (151 mg, 372 μmol) were added to the flask and dried further *in vacuo* at r.t. for 12 h. Polymerization was carried out at 160 ºC for 12 h by heating the flask in an oil bath. The product was purified by reprecipitation using chloroform (100 mL) as a good solvent and diethyl ether

(1000 mL) as a poor solvent to obtain the PCGA-PEG-PCGA triblock copolymer as a colorless liquid or white solid. The yield after reprecipitation was 52.3 g (92.7%). Various PCGA-PEG-PCGA triblock copolymers were synthesized by changing CL and GL feed amounts and the MW of PEG (using PEG_{1000} or PEG_{2000}). The products were analyzed using ^{1}H-NMR, and the CL/GA ratio (GL corresponds two GA units) was determined from the ^{1}H-NMR spectra. The obtained PCGA-PEG-PCGA triblock copolymers (ABA series) were given code names such as ABA1.5k-3.1k-3.4, where 1.5k = MW of a PEG segment, 3.1k = sum MW of two PCGA segments, and 3.4 = molar ratio of CL/GA in a PCGA segment. Typical ^{1}H-NMR spectra and SEC elution profiles for ABA triblock copolymers are shown in **Figures S1(a)–(k)**.

Synthesis of PEG-PCGA-PEG (BAB triblock copolymer)

AB-type diblock copolymers of PEG and PCGA (PEG-PCGA) were synthesized by ring-opening copolymerization of CL and GL in the presence of MeO-PEG_{550} as a macroinitiator and $Sn(Oct)_2$ as a catalyst according to the method described below (**Scheme S2**). MeO-PEG_{550} (9.42 g, 17.1 mmol) was dried *in vacuo* at 120 ºC for 5 h in a 100-mL flask with a stopcock. After cooling to r.t., CL (18.0 g, 158 mmol), GL (2.62 g, 22.5 mmol), and $Sn(Oct)_2$ (79.8 mg, 197 μmol) were added to the flask and dried further *in vacuo* at r.t. for 12 h. Polymerization was carried out at 160 ºC for 12 h by heating the flask in an oil bath. The product was purified using the same reprecipitation method described above. A white solid or colorless liquid of PEG-PCGA diblock copolymer was obtained. Yield: 18.4 g (61.5%). Various PEG-PCGA diblock copolymers were synthesized by changing CL and GL feed amounts. The obtained PEG-PCGA (4.50 g, 2.14 mmol) was placed in a flask and dried *in vacuo* at 120 ºC for 4 h. Anhydrous dichloromethane was added to the flask to dissolve PEG-PCGA. HMDI (183 mg, 1.09 mmol) was dissolved in anhydrous dichloromethane and refluxed at 70 °C for 6 h. The product was purified using the same reprecipitation method described above. A white solid (in some cases, a pale-yellow solid or liquid) of the PEG-PCGA-PEG triblock copolymer was obtained. The yield after reprecipitation was 3.14 g (68.3%). The obtained PEG-PCGA-PEG triblock copolymers (BAB series) were given code names such as BAB1.1k-3.8k-3.9, where 1.1k = sum MW of two PEG segments and 3.8k = MW of the PCGA segment, and the molar ratio of CL/GA in the PCGA segment is 3.9. Typical ^{1}H-NMR spectra and SEC elution profiles for BAB triblock copolymers are shown in **Figures S2(a)–(f)**.

Synthesis of ABA-Ac and ABA-Bu series

The introduction of an acetyl or butyryl group on the termini of PCGA-PEG-PCGA was carried out under an N_2 atmosphere, as shown in **Scheme S3**. The previously prepared ABA1.5k-3.1k-3.4 (0.87 g, 0.19 mmol) was placed in a 30-mL flask and dried *in vacuo* for 2h. Pyridine (3 mL) was added to the flask to dissolve the polymer. Ac_2O (17.8 μL, 0.19 mmol) and DMAP (33.0 mg, 0.27 mol) were

then added to the flask. The reaction mixture was stirred at 80 °C for 1 h. Pyridine, excess Ac_2O, and acetic acid by-products were removed under reduced pressure. The product was purified by reprecipitation using chloroform (1.5 mL) as a good solvent and a mixture of diethyl ether and methanol (10/1, v/v) (30 mL) or diethyl ether (30 mL) as a poor solvent to give a white solid of the partially acetylated PCGA-PEG-PCGA, ABA-Ac series. The yield after reprecipitation was 0.53 g (67.1%). By varying the feed ratio of Ac_2O or butyric acid anhydride, PCGA-PEG-PCGA polymers with various degrees of substitution (DS) of the acetyl or butyryl groups (ABA-Ac or ABA-Bu series) were synthesized. The products were analyzed using ^{1}H-NMR, and the DS values of the acetyl or butyryl groups were calculated from the ^{1}H-NMR spectra. The obtained partially acetylated or butyrylated PCGA-PEG-PCGAs were given code names such as ABA-Ac_{96} or ABA-Bu_{91}, where 96 or 91 = DS of acetyl or butyryl groups, respectively. Typical ^{1}H-NMR spectra and SEC elution profiles for ABA-Ac and ABA-Bu series are shown in **Figures S3(a)–(d), S4(a)–(b)**.

Synthesis of 4-arm PEG-PCGA and partially acetylated 4-arm PEG-PCGA

4-Arm PEG-PCGA and partially acetylated 4-arm PEG-PCGA were synthesized using a method similar to that described above, using 4-arm PEG_{5000} as a macroinitiator and subsequent acetylation (**Scheme S4**).

4-Arm PEG_{5000} (1.49 g, 0.298 mmol) was dried *in vacuo* at 120 ºC for 3 h in a 30-mL flask with a stopcock. After cooling to r.t., CL (3.29 g, 28.9 mmol), GL (0.577 g, 4.97 mmol), and $Sn(Oct)_2$ (17.9 mg, 44.2 μmol) were added to the flask. The flask was then cooled with liquid N_2 and dried overnight *in vacuo*. Polymerization was performed at 160 °C for 12 h by heating the flask in an oil bath. The product was purified by the same reprecipitation method. A white or pale-yellow solid of 4-arm PEG-PCGA was obtained. The yield after reprecipitation was 4.33g (80.3%). Various 4-arm PEG-PCGAs were synthesized by varying CL and GL feed amounts. The products were analyzed using ^{1}H-NMR, and the CL/GA ratio was determined from the ^{1}H-NMR spectra. The obtained 4-arm PEG-PCGAs (4-arm series) were given code names such as 4-arm5.0k-7.6k, where 5.0k = MW of 4-arm PEG and 7.6k = sum MW of four PCGA segments. Typical ^{1}H-NMR spectra and SEC elution profiles for 4-arm series are shown in **Figures S5(a)–(d)**.

The prepared 4-arm5.0k-7.6k (0.60 g, 0.047 mmol) was placed in a 30-mL flask and dried *in vacuo* for 2h. Pyridine (3 mL) was added to the flask to dissolve the polymer. Ac_2O (26.8 μL, 0.071 mmol) was then added. The reaction mixture was stirred at 80 °C for 1 h. Pyridine, excess Ac_2O, and acetic acid by-products were removed under reduced pressure. The product was purified by the same precipitation method. A white solid, partially acetylated 4-arm PEG-PCGA, was obtained. The yield after reprecipitation was 0.56 g (93.1%). By varying the amount of Ac_2O, partially acetylated 4-arm PEG-PCGA with various DS of acetyl groups (4-arm-Ac series) were synthesized. The products were analyzed using ^{1}H-NMR, and the DS values of the acetyl groups were calculated from the ^{1}H-NMR

spectra. The obtained partially acetylated 4-arm PEG-PCGAs (4-arm-Ac series) were named 4-arm-Ac_{18}, where 18 = DS of the acetyl group. Typical ^{1}H-NMR spectra and SEC elution profiles for 4-arm-Ac series are shown in **Figures S6(a)–(d)**.

Morphology of the polymers

For the polymer morphology, photographs of the neat polymers (in dry state at r.t.) are shown in **Figures S7–12**. No photograph was recorded for the samples not shown.

Confirmation of sol-to-gel transition behavior

The sol-to-gel transition behavior of the aqueous solutions of the polymers was investigated by a test-tube inverting method.[4] A vial containing the polymer dissolved in phosphate-buffered saline (PBS, pH = 7.4) was immersed in a water bath at the desired temperature for 15 min, removed from the water bath, then inverted repeatedly within 30 sec to determine T_{gel} based on the criteria of ‘‘flow’’ (= sol) and ‘‘no flow’’ (= gel). This was repeated with a temperature increment of 1 °C per step. The measurements were repeated thrice at each temperature to determine the transition temperature in the phase diagram. Typical phase diagrams for the polymers are shown in **Figure S13**. Polymer concentrations were 20 wt.% for determine transition temperature in Table S1-S5, otherwise cited.

Temperature-dependent rheological measurements of the temperature-responsive sol-to-gel transition of the polymer solution in PBS (pH = 7.4) were performed using a dynamic rheometer (Thermo HAAKE RS600, Thermo Fisher Scientific, Waltham, MA, USA). A solvent trap was used to prevent solvent vaporization. The polymer concentration was 30 wt. %. Typically, each sample was placed between parallel plates (25 mm diameter and 1.0 mm gap) using a syringe. The data was collected under controlled stress (4.0 dyn/cm^2) at a frequency of 1.0 rad/s. The heating rate was 0.5 °C/min. The storage modulus (G’) and loss modulus (G’) of the formulations were monitored in the range of 20-50 °C, and the gelation temperature (T_{gel}) was defined as the crossover point from G’ to G”. Typical rheological measurements are shown in **Figure S14**.

Table S1. Characterization of PEG-PCGA-PEG triblock copolymers (BAB series)

Code	MW of PEG (g/mol) [a)]	MW of PCGA (g/mol) [b)]	CL/GA (mol/mol) [c)]	Total M_n (g/mol) [d)]	M_w/M_n [e)]	PCGA%[f)]	Morphology	T_{gel} (ºC) [g)]	Other transition temperature (ºC) [h)]
BAB1.1k-2.1k-2.4	550 × 2	2100	2.4	3200	1.5	65.6	Viscous liquid	N.D.	53 [i)]
BAB1.1k-2.5k-4.4		2500	4.4	3600	1.6	69.4	Sticky solid	N.D.	52 [i)]
BAB1.1k-2.9k-3.6		2900	3.6	4000	1.5	72.5	Sticky solid	N.D.	52 [i)]
BAB1.1k-3.3k-1.5		3300	1.5	4400	1.5	75.0	Viscous liquid	47	53[j)], 57[i)]
BAB1.1k-3.4k-3.5		3400	3.5	4500	1.3	75.6	Powdery solid	43	54 [k)]
BAB1.1k-3.7k-4.7		3700	4.7	4800	1.3	77.1	Sticky solid	45	56 [k)]
BAB1.1k-3.8k-3.9		3800	3.9	4900	1.3	77.6	Powdery solid	42	58 [k)]
BAB1.1k-4.0k-3.1		4000	3.1	5100	1.5	78.4	Sticky solid	41	55 [k)]
BAB1.1k-4.3k-3.7		4300	3.7	5400	1.6	79.6	Powdery solid	N.D.	45 [i)]
BAB1.1k-4.9k-3.9		4900	3.9	6000	1.3	81.7	Powdery solid	N.D.	37 [i)]
BAB1.1k-5.6k-3.5		5600	3.5	6700	–	83.6	Powdery solid	– (insoluble)	– (insoluble)

a) as indicated by the supplier.
b) total molecular weight of PCGA segment connected with urethane bonds estimated by ^{1}H-NMR.
c) molar ratio of CL to GA found in the polymer, estimated by ^{1}H-NMR.
d) number-average molecular weight estimated by ^{1}H-NMR.
e) polydispersity index estimated by SEC.
f) Weight content of PCGA segment = [(MW of total polymer) - (MW of PEG unit)] / (MW of total polymer) × 100 (%)
g) sol-to-gel transition temperature determined by test tube inverting method.
h) transition temperature other than sol-to-gel shown as i)-k).
i) sol-to-precipitate transition.
j) gel-to-sol transition.
k) gel-to-precipitate transition.
N.D.: not detected, —: not determined.

Table S2. Characterization of partially acetylated or butyrylated PCGA-PEG-PCGA triblock copolymers (ABA-Ac series and ABA-Bu series)

Code	Terminal group	DS of terminal groups (%) [b]	Morphology	T_{gel} (ºC) [c]	T_{sol} (ºC) [d]	T_{prec} (ºC) [e]
ABA-Ac$_0$ (ABA1.5k-3.1k-3.4) [a]	*None* (-OH)	0	Powdery solid	42	45	53
ABA-Ac$_{22}$	acetyl	22.3	Powdery solid	40	45	57
ABA-Ac$_{36}$		36.5	Powdery solid	37	45	51
ABA-Ac$_{52}$		52.0	Powdery solid	36	46	54
ABA-Ac$_{96}$		95.8	Sticky solid	34	48	51
ABA-Bu$_{12}$	butyryl	12.0	Powdery solid	39	44	53
ABA-Bu$_{36}$		35.7	Powdery solid	35	44	50
ABA-Bu$_{46}$		46.0	Powdery solid	33	46	50
ABA-Bu$_{69}$		68.7	Powdery solid	29	N.D.	38 [f]
ABA-Bu$_{82}$		82.3	Powdery solid	22	N.D.	35 [f]
ABA-Bu$_{89}$		89.2	Powdery solid	18	N.D.	34 [f]
ABA-Bu$_{91}$		91.3	Powdery solid	16	N.D.	34 [f]

a) base polymer used to prepare ABA-Ac and ABA-Bu; MW of PEG = 1540, MW of PCGA = 1550 × 2, CL/GA ratio = 3.4, total M_n = 4640, M_w/M_n = 1.3
b) degree of substitution of acetyl or butyryl groups (%).
c) sol-to-gel transition temperature determined by test tube inverting method.
d) gel-to-sol transition.
e) sol-to-precipitate transition otherwise cited.
f) gel-to-precipitate transition.
N.D.: not detected.

Table S3. Characterization of 4-arm PEG-PCGA copolymers (4-arm series)

Code [a]	MW of PCGA (g/mol)[b]	CL/GA (mol/mol)[c]	Total M_n (g/mol)[d]	M_w/M_n[e]	PCGA%[f]	Morphology	T_{gel} (°C)[g]	T_{prec} (°C)[h]
4-arm5.0k-3.6k	900 × 4	4.1	8600	1.5	42	Sticky solid	N.D.	60[i]
4-arm5.0k-7.2k	1800 × 4	3.6	12 200	1.6	59	Sticky solid	57	60
4-arm5.0k-7.6k	1900 × 4	3.4	12 600	1.9	60	Powdery solid	53	57
4-arm5.0k-8.0k	2000 × 4	4.1	13 000	1.7	62	Powdery solid	52	58
4-arm5.0k-8.8k	2200 × 4	3.8	13 800	1.9	64	Powdery solid	63	66
4-arm5.0k-12.0k	3000 × 4	3.4	17 000	2.2	71	Powdery solid	41	58
4-arm5.0k-12.4k	3100 × 4	3.3	17 400	2.0	71	Powdery solid	47	55
4-arm5.0k-13.6k	3400 × 4	3.2	18 600	1.1	73	Powdery solid	42	51
4-arm5.0k-16.0k	4000 × 4	3.2	21 000	1.1	76	Powdery solid	41	64
4-arm5.0k-20.0k	5000 × 4	4.0	25 000	2.5	80	Powdery solid	– (insoluble)	– (insoluble)

a) MW of 4-arm PEG = 5000.
b) estimated by ^{1}H-NMR.
c) molar ratio of CL to GA found in the polymer, estimated by ^{1}H-NMR.
d) number-average molecular weight estimated by ^{1}H-NMR.
e) polydispersity index estimated by SEC.
f) weight content of PCGA segment = [(MW of total polymer) - (MW of PEG unit)] / (MW of total polymer) × 100 (%)
g) sol-to-gel transition temperature determined by test tube inverting method.
h) gel-to-precipitate transition otherwise cited.
i) sol-to-precipitate transition.
N.D.: not detected, —: not determined.

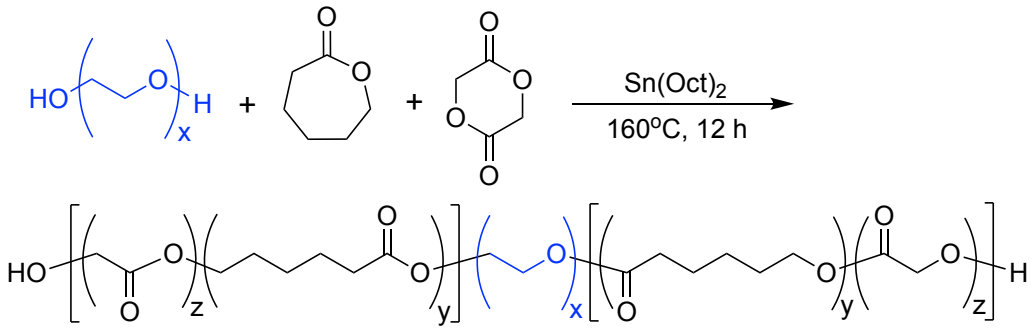
Table S4. Characterization of partially acetylated 4-arm PEG-PCGA copolymers (4-arm-Ac series)

Code	DS of acetyl group[b)]	Morphology	T_{gel} (ºC) [c)]	T_{prec} (ºC) [d)]
4-arm-Ac$_0$ (4-arm5.0k-7.6k) [a)]	0.0	Powdery solid	53	57
4-arm-Ac$_{18}$	17.5	Powdery solid	49	62
4-arm-Ac$_{38}$	37.6	Sticky solid	49	65
4-arm-Ac$_{56}$	56.5	Sticky solid	46	65
4-arm-Ac$_{66}$	65.7	Sticky solid	44	64
4-arm-Ac$_{95}$	94.7	Powdery solid	44	61

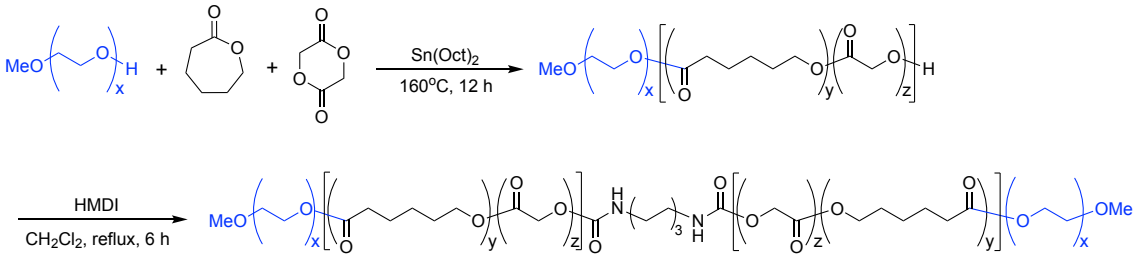
a) base polymer used to prepare 4-arm-Ac; MW of 4-arm PEG = 5000, MW of PCGA = 1900 × 4, CL/GA ratio = 3.4, total M_n = 12600, M_w/M_n = 1.9
b) degree of substitution of acetyl groups (%).
c) sol-to-gel transition temperature determined by test tube inverting method.
d) gel-to-precipitate transition.

Table S5. Results of differential scanning calorimeter (DSC) analysis for PCGA-PEG-PCGA triblock copolymers (ABA series) and PEG-PCGA-PEG triblock copolymers (BAB series)

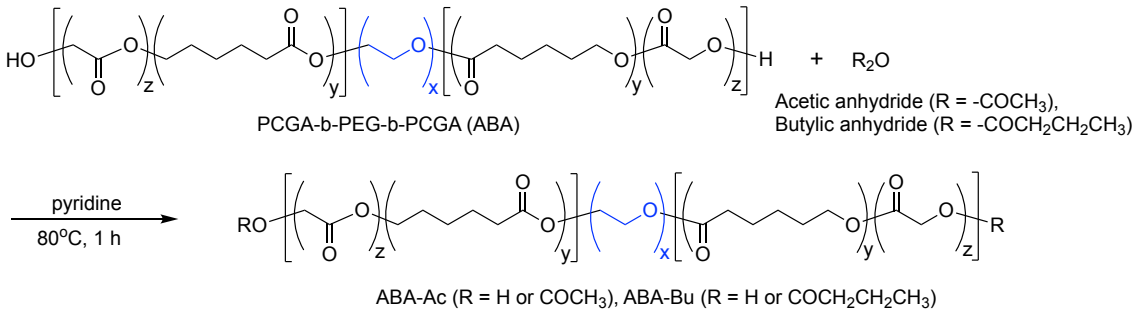
Code	mp_1 [ºC]	ΔH_1 [J/g]	mp_2 [ºC]	ΔH_2 [J/g]	mp_3 [ºC]]	ΔH_3 [J/g]	ΔH_{total} [J/g]	PCGA%	CL%	Xc [%]	T_{gel} [ºC]	Morphology
ABA1.5k-3.1k-3.4	23.0	46.0	-	-	-	-	46.0	66.8	52.1	63.3	42	Powdery solid
ABA1.5k-3.5k-3.4	21.9	44.3	-	-	-	-	44.3	66.9	54.1	58.7	38	Powdery solid
ABA1.5k-3.8k-3.1	22.6	16.4	27.4	1.0	-	-	17.4	71.2	54.2	23.0	33	Powdery solid
ABA1.5k-3.8k-3.5	20.7	13.5	27.7	4.4	-	-	17.9	71.2	55.8	23.0	33	Powdery solid
ABA1.5k-4.0k-3.7	20.9	15.5	34.5	2.0	-	-	17.5	72.2	57.3	21.9	33	Powdery solid
ABA1.5k-4.6k-3.5	21.8	11.4	30.1	9.9	-	-	21.3	74.9	58.7	26.0	insoluble	Powdery solid
BAB1.1k-3.3k-1.5	9.6	0.4	-	-	-	-	0.4	75.0	45.0	0.6	47	Viscous liquid
BAB1.1k-3.4k-3.5	22.1	5.7	29.6	5.4	-	-	11.1	75.6	58.8	13.5	43	Powdery solid
BAB1.1k-3.8k-3.9	27.1	8.5	35.5	17.8	-	-	26.3	77.6	61,7	30.6	42	Powdery solid
BAB1.1k-4.0k-3.1	14.0	0.9	21.3	1.0	29.8	14.5	16.4	78.4	59.3	19.8	41	Sticky solid



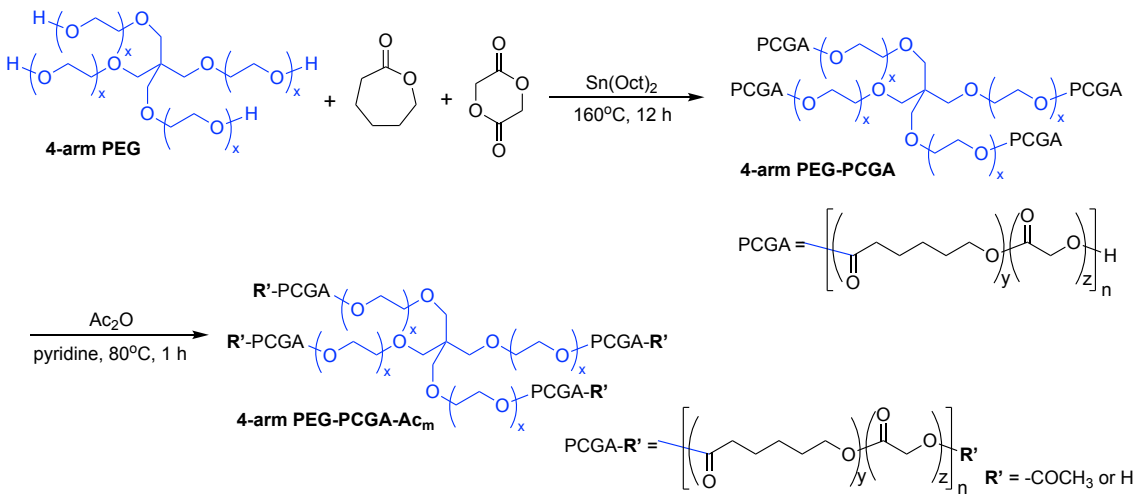
Scheme S1. Synthesis of PCGA-PEG-PCGA triblock copolymers (ABA series).



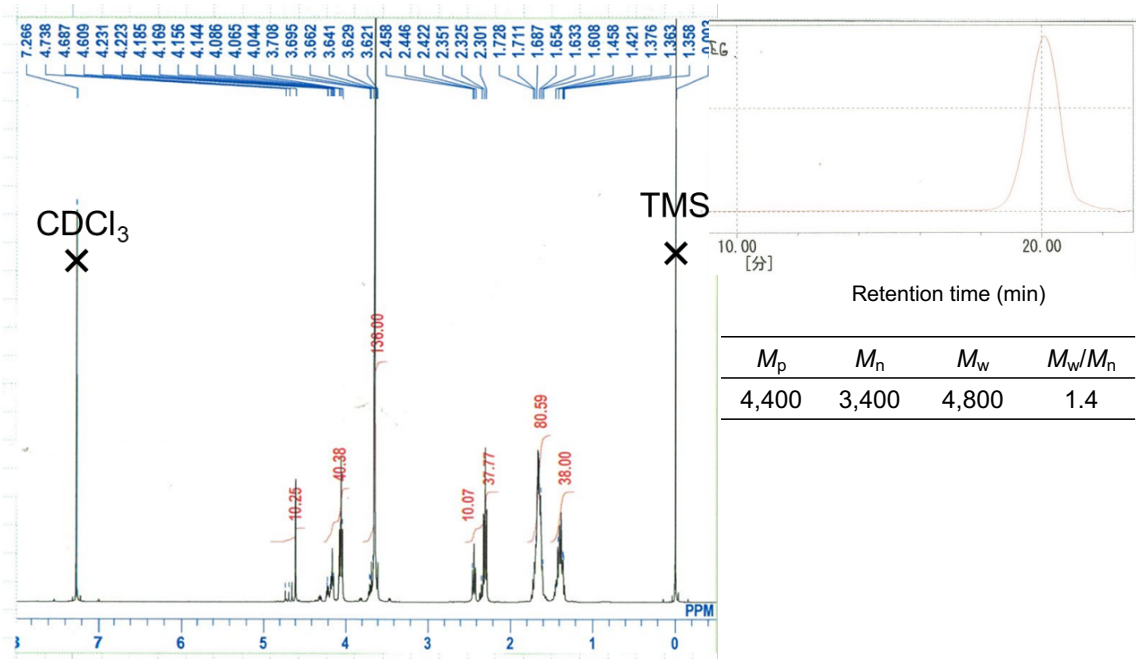
Scheme S2. Synthesis of PEG-PCGA-PEG triblock copolymer (BAB series).



Scheme S3. Synthesis of partially acetylated or butyrylated PCGA-PEG-PCGA (ABA-Ac series and ABA-Bu series).

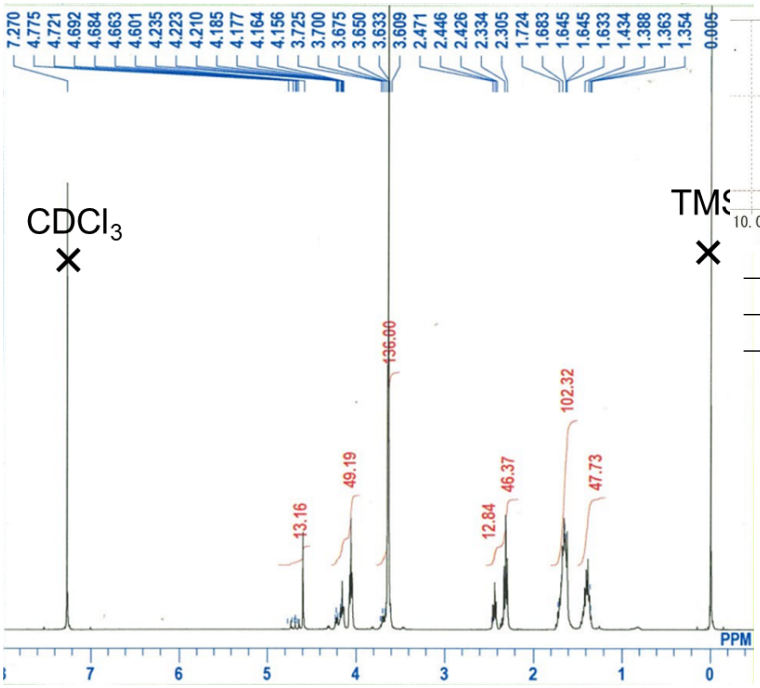


Scheme S4. Synthesis of 4-arm PEG-PCGA (4-arm series) and partially acetylated 4-arm PEG-PCGA (4-arm-Ac series).



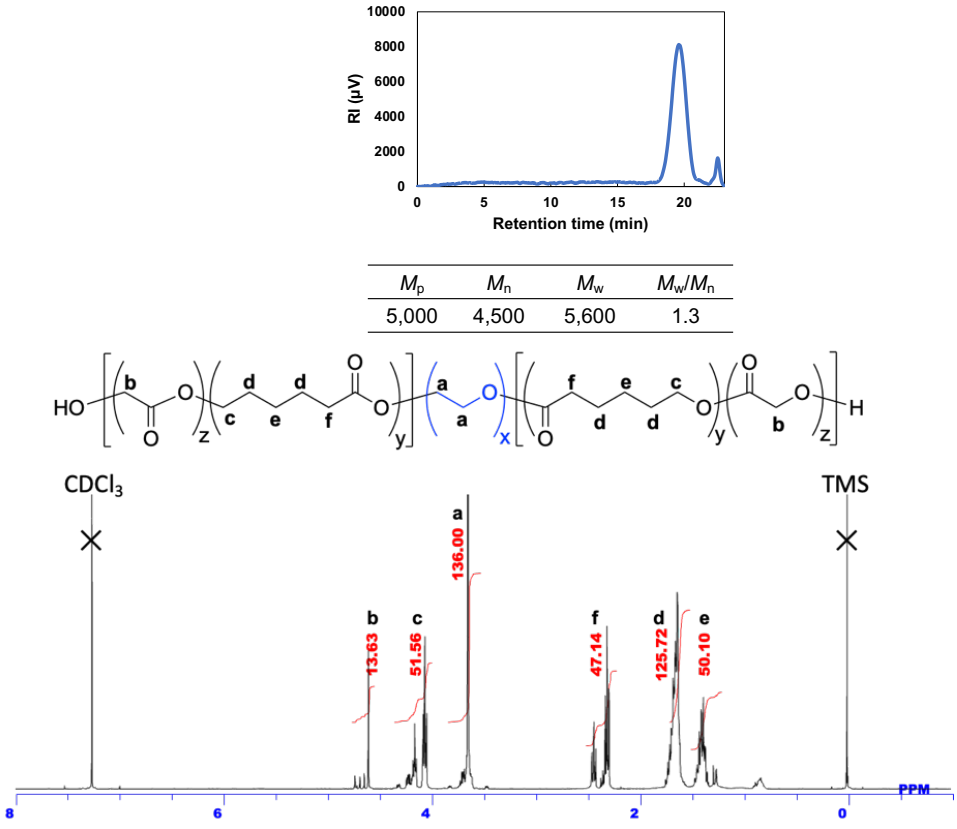
M_p	M_n	M_w	M_w/M_n
4,400	3,400	4,800	1.4

Figure S1(a). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.5k-2.4k-3.6.



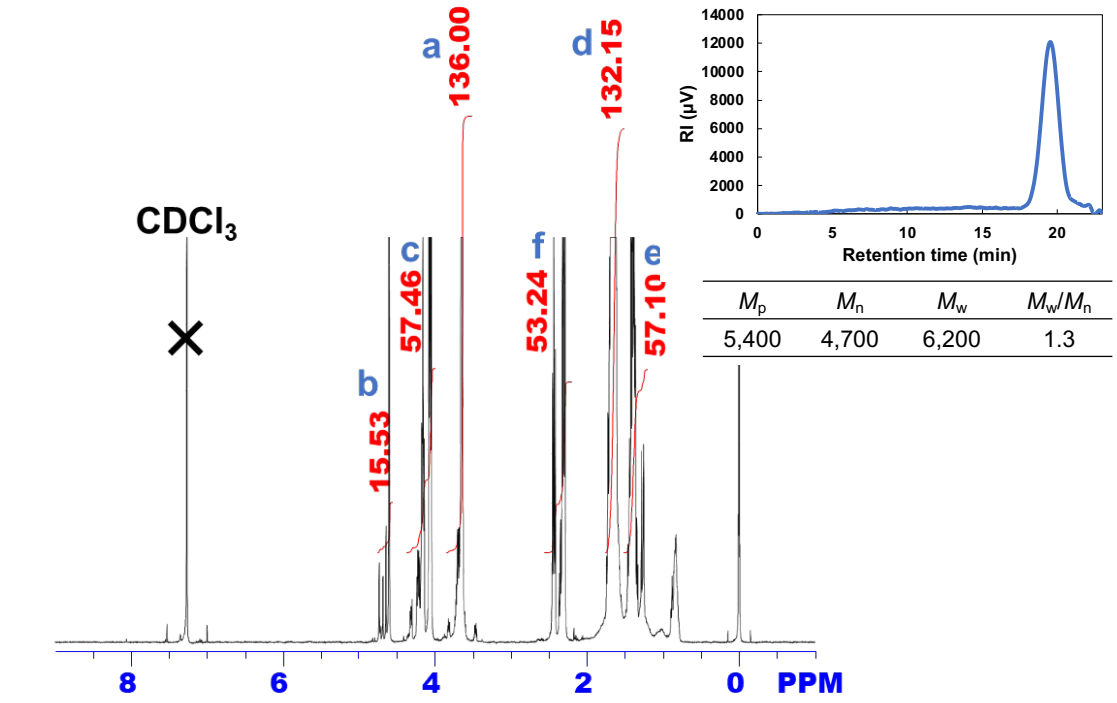
M_p	M_n	M_w	M_w/M_n
5,100	3,900	5,600	1.4

Figure S1(b). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.5k-3.0k-3.5.



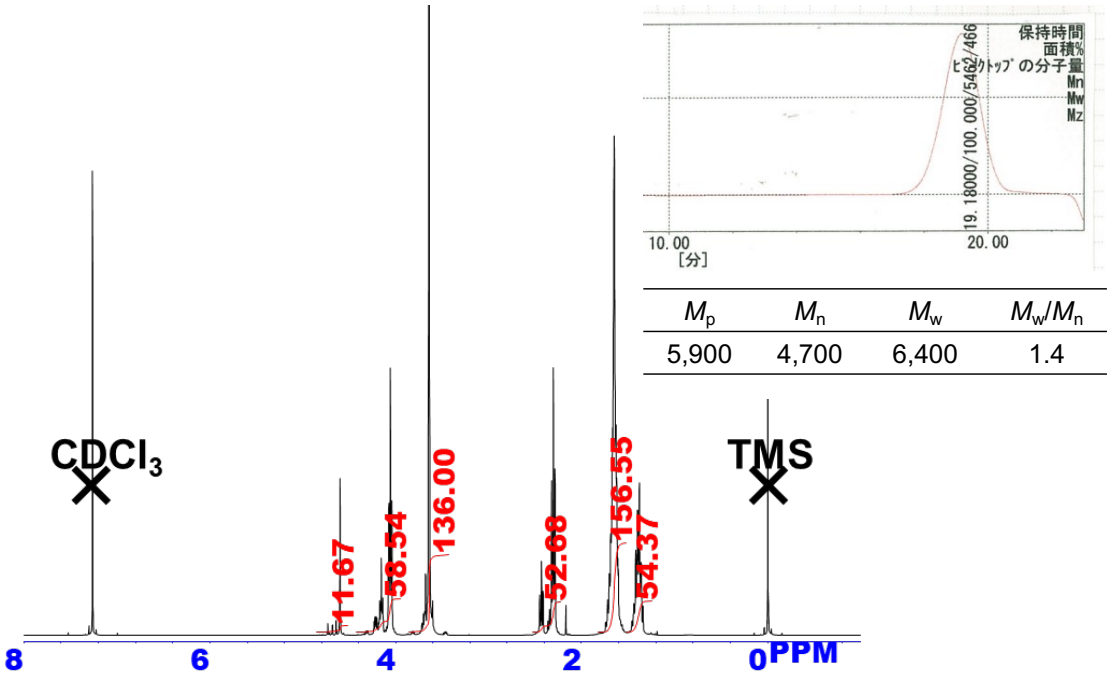
M_p	M_n	M_w	M_w/M_n
5,000	4,500	5,600	1.3

Figure S1(c). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.5k-3.1k-3.4.



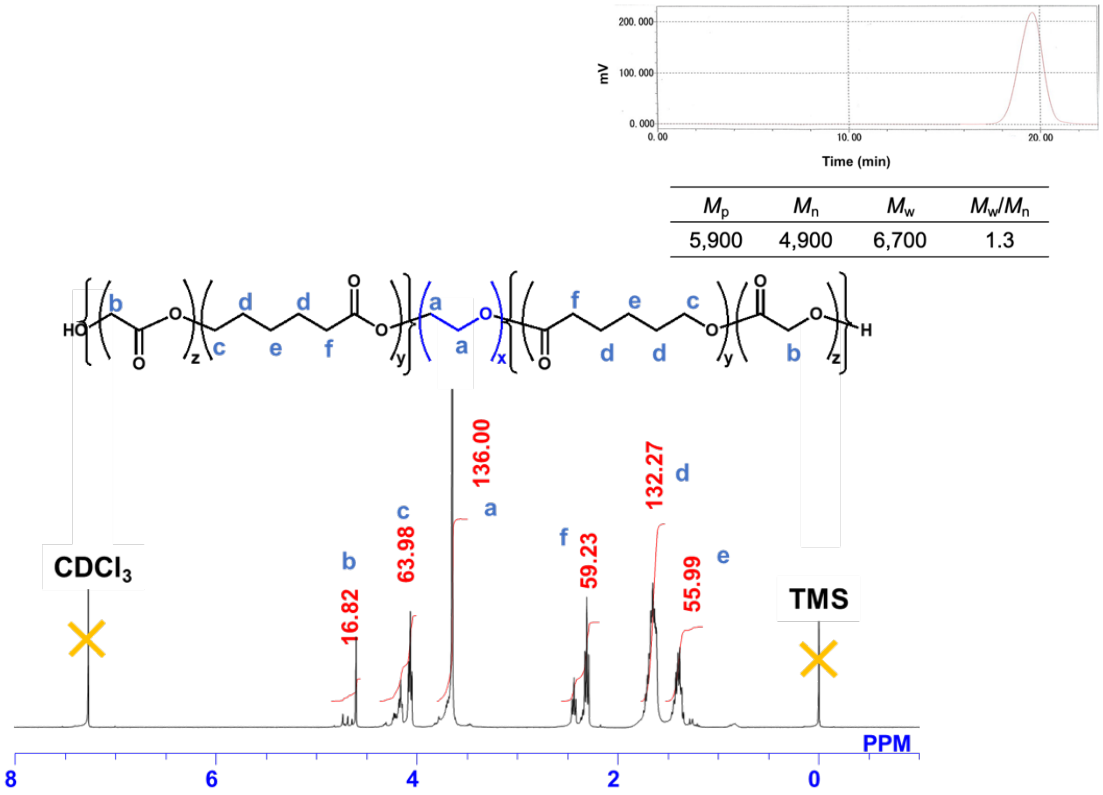
M_p	M_n	M_w	M_w/M_n
5,400	4,700	6,200	1.3

Figure S1(d). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.5k-3.5k-3.4.



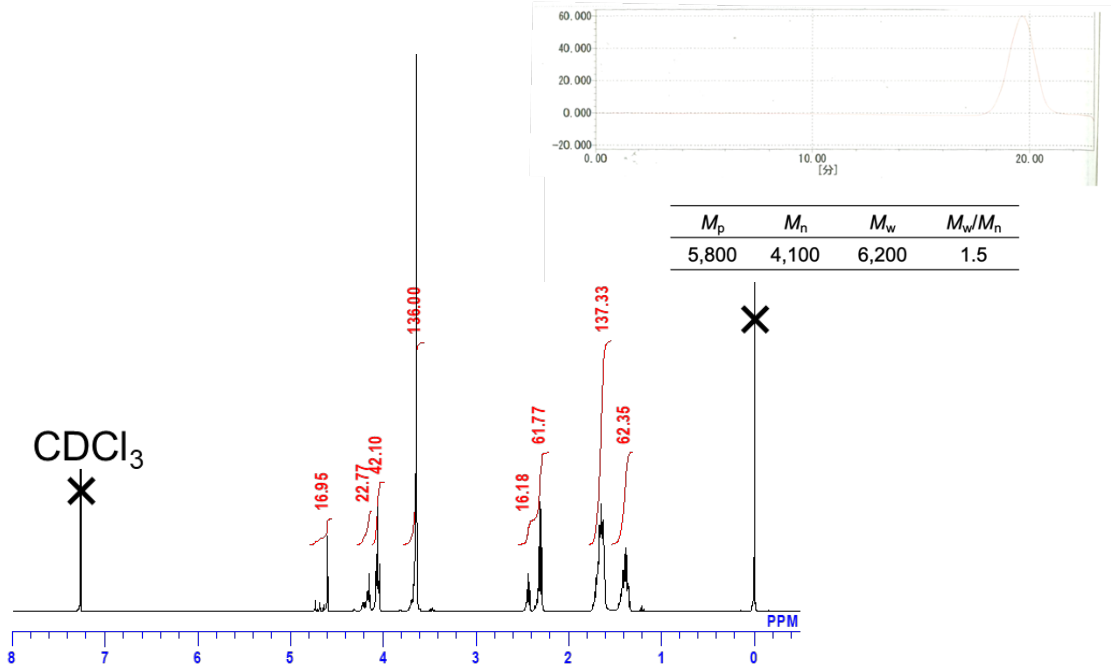
M_p	M_n	M_w	M_w/M_n
5,900	4,700	6,400	1.4

Figure S1(e). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.5k-3.6k-4.8.



M_p	M_n	M_w	M_w/M_n
5,900	4,900	6,700	1.3

Figure S1(f). ^{11}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.5k-3.8k-3.5.



M_p	M_n	M_w	M_w/M_n
5,800	4,100	6,200	1.5

Figure S1(g). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.5k-4.0k-3.7.

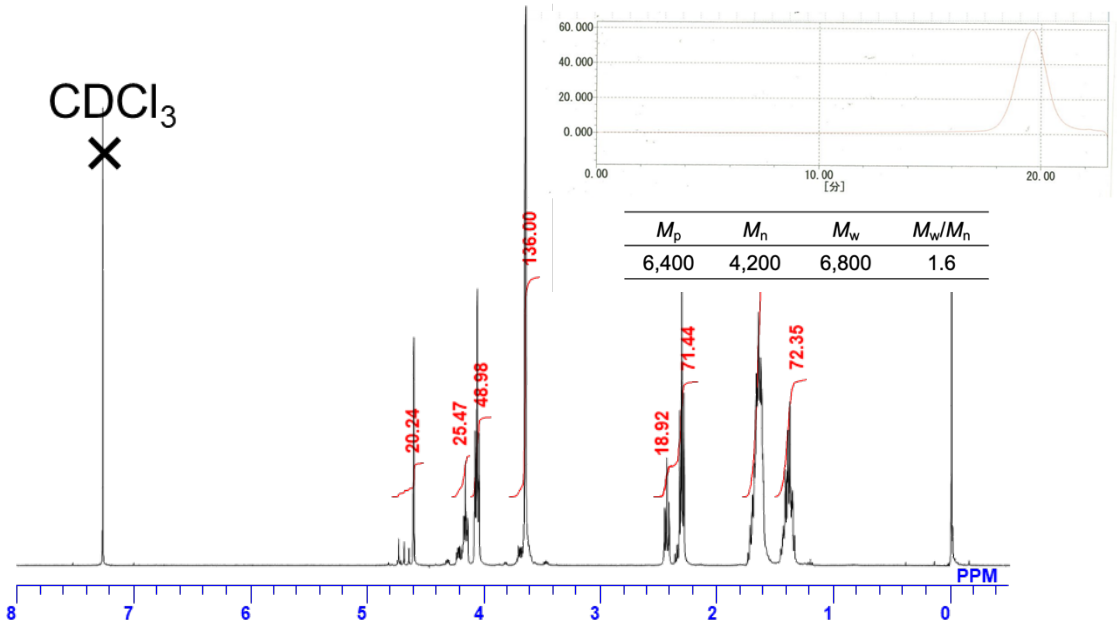


Figure S1(h). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.5k-4.6k-3.5.

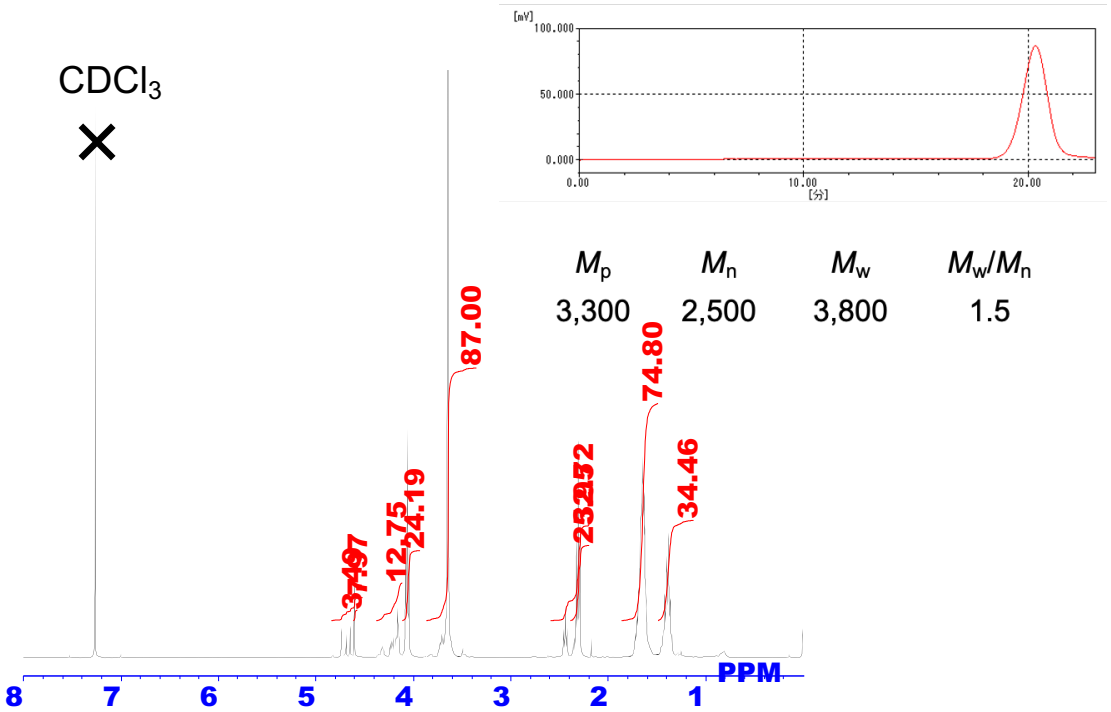


Figure S1(i). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.0k-2.0k-4.1.

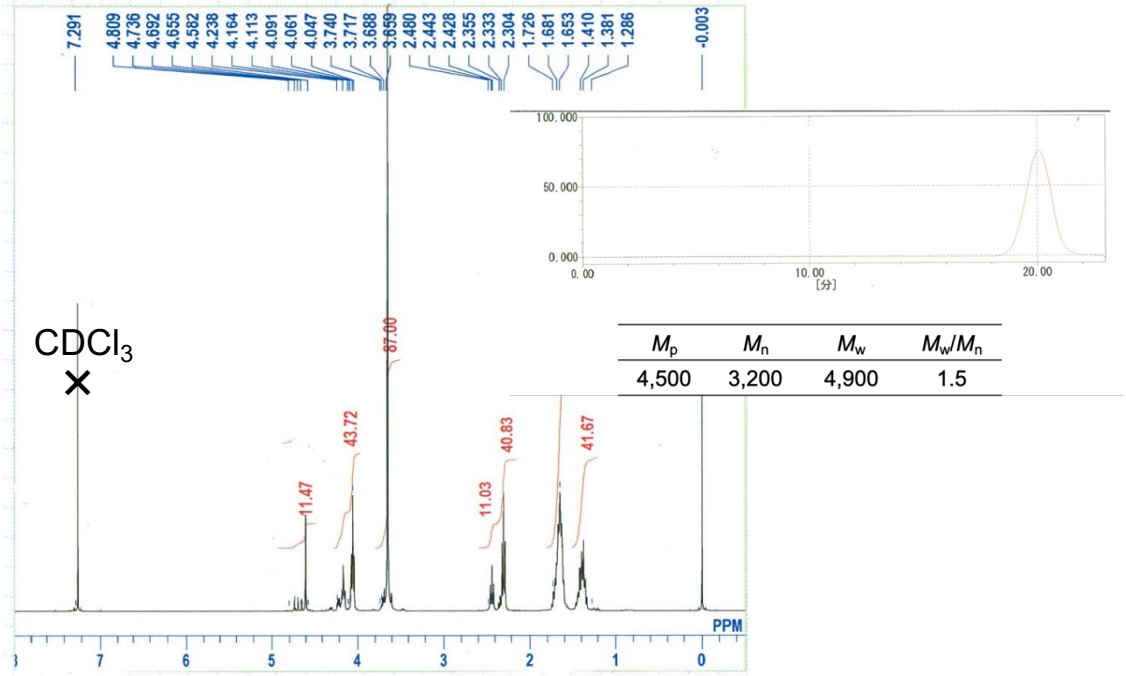


Figure S1(j). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA1.0k-2.6k-3.6.

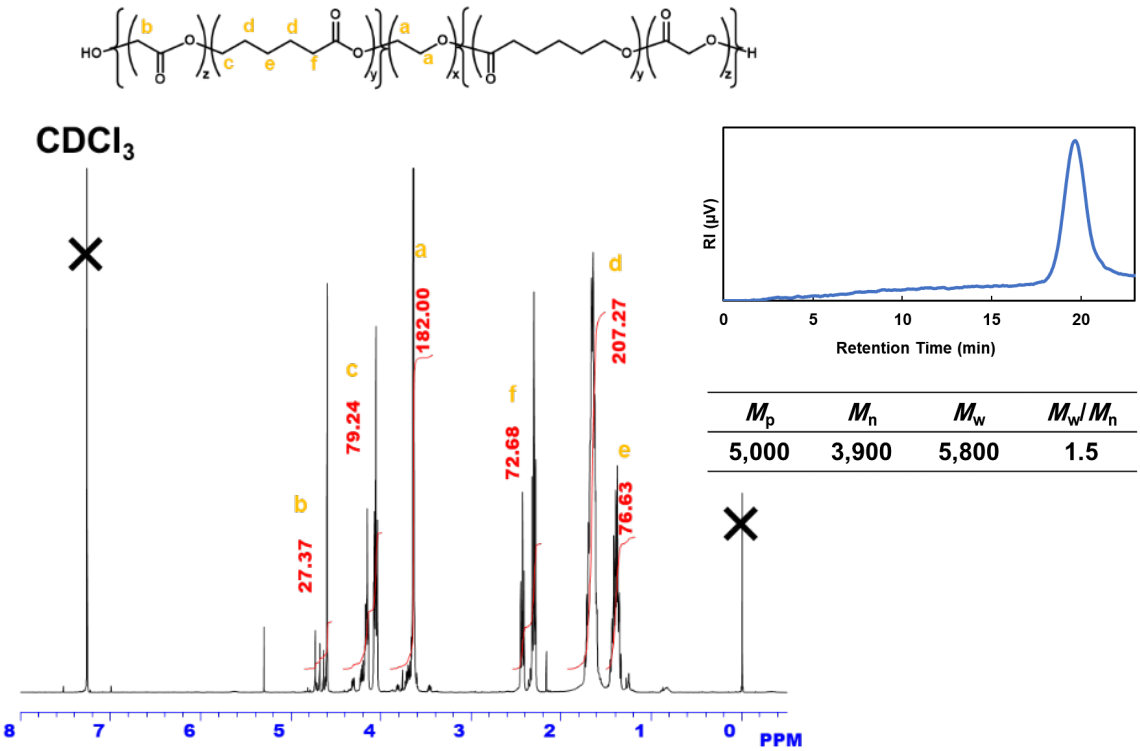
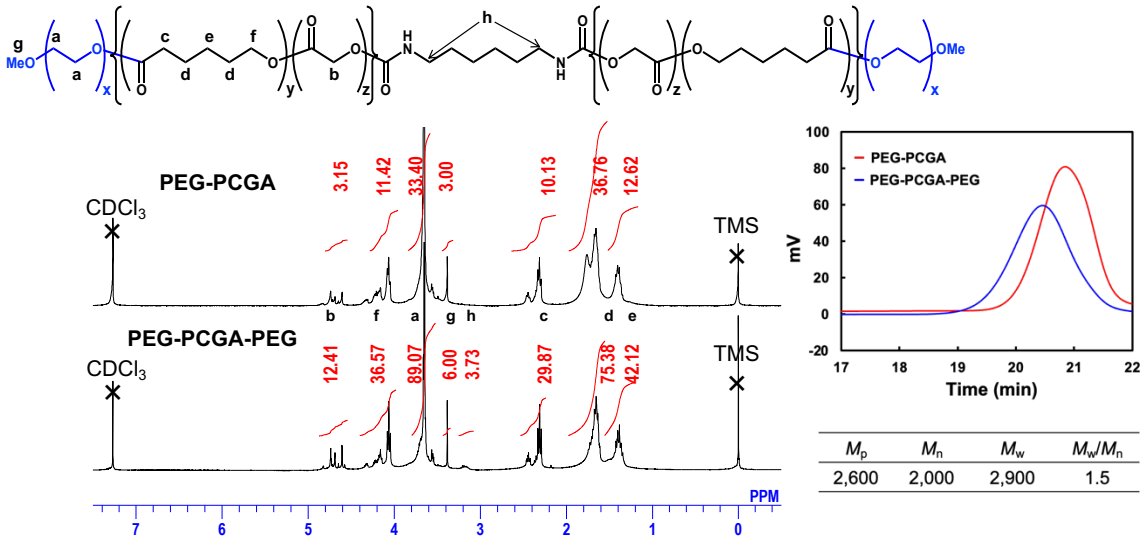
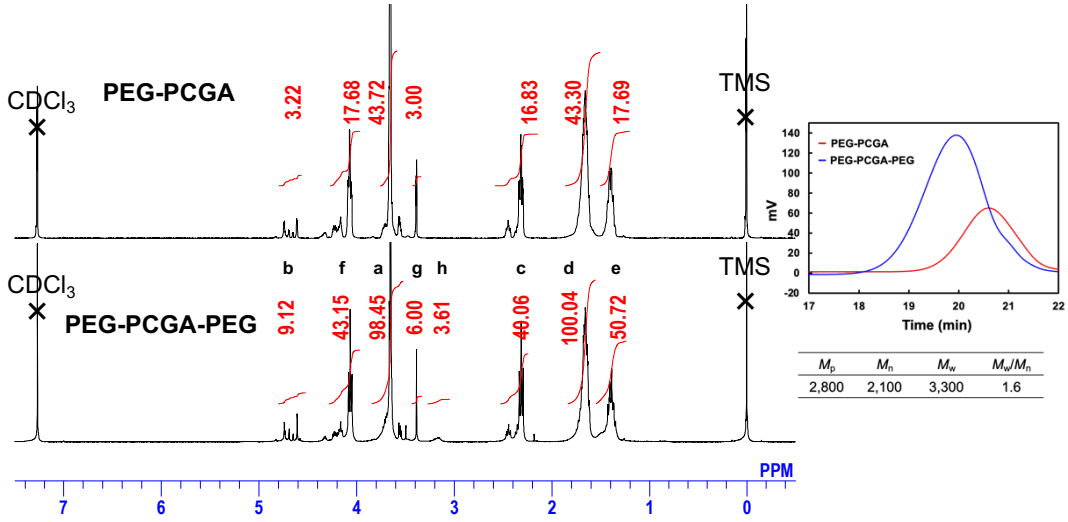


Figure S1(k). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA2.0k-4.6k-2.7.



M_p	M_n	M_w	M_w/M_n
2,600	2,000	2,900	1.5

Figure S2(a). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for BAB1.1k-2.1k-2.4.



M_p	M_n	M_w	M_w/M_n
2,800	2,100	3,300	1.6

Figure S2(b). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for BAB1.1k-2.5k-4.4.

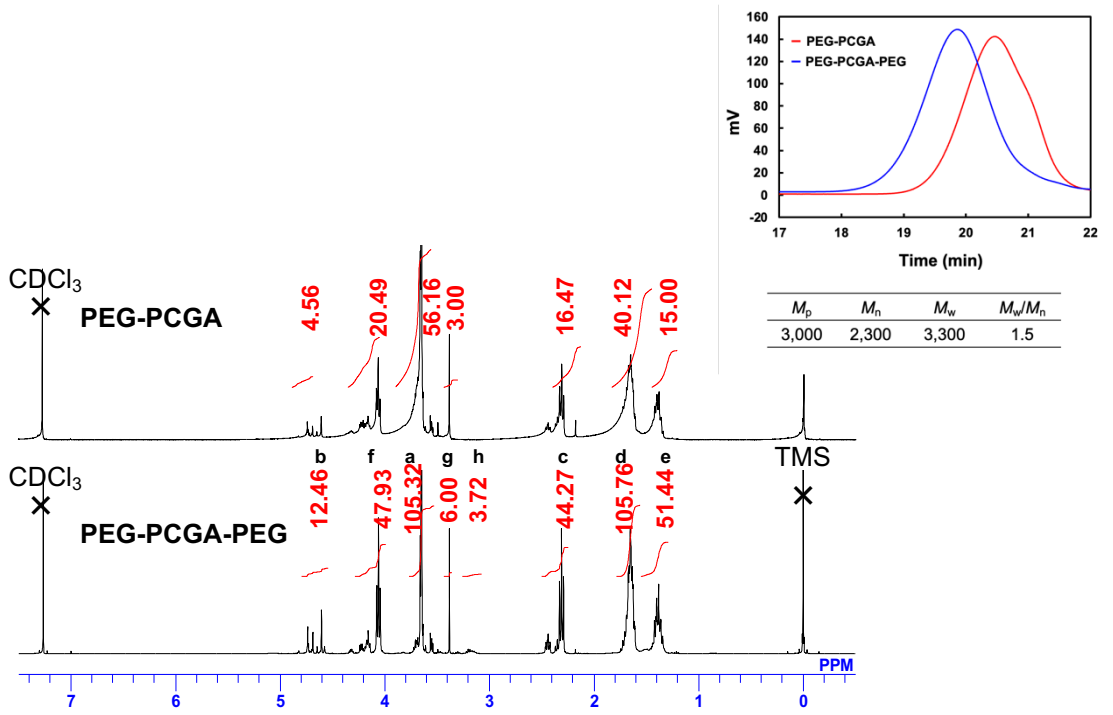


Figure S2(c). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for BAB1.1k-2.9k-3.6.

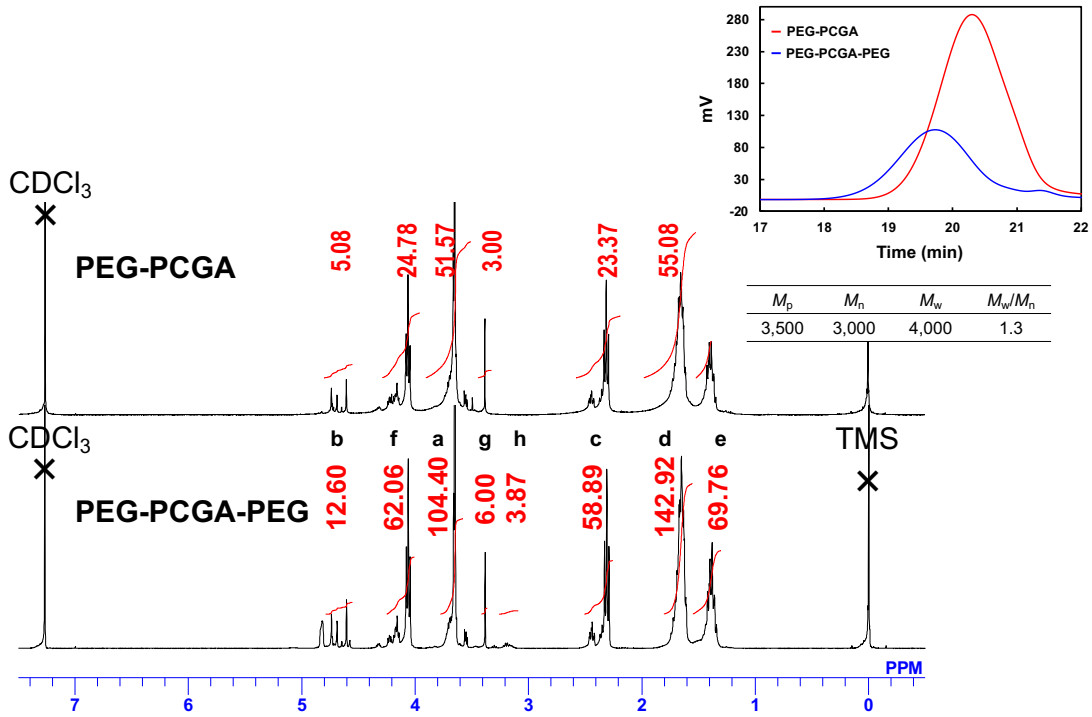
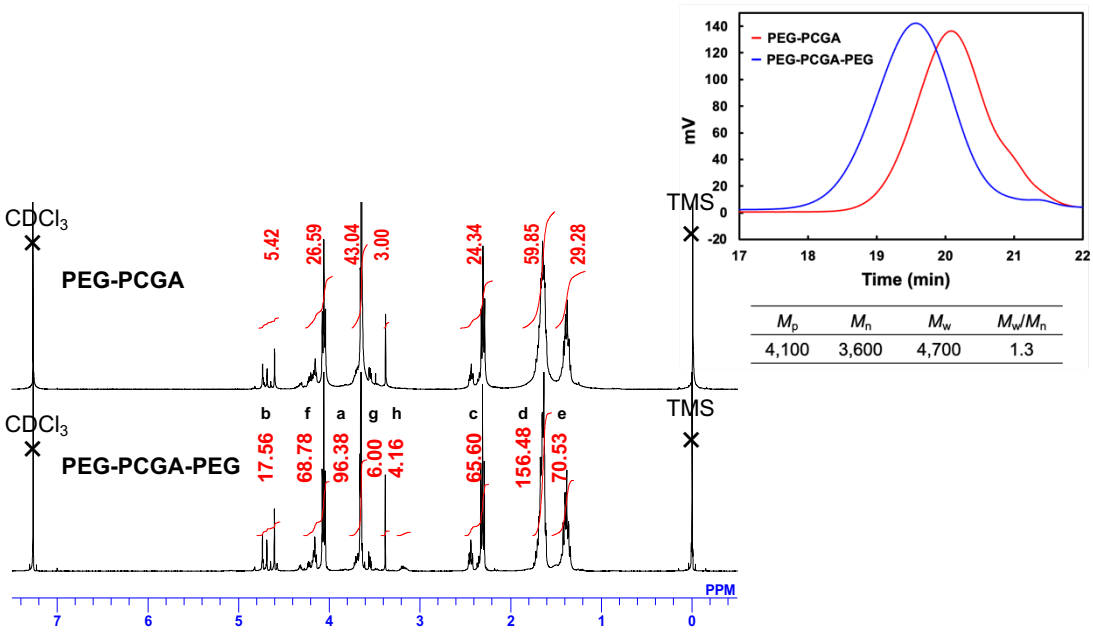
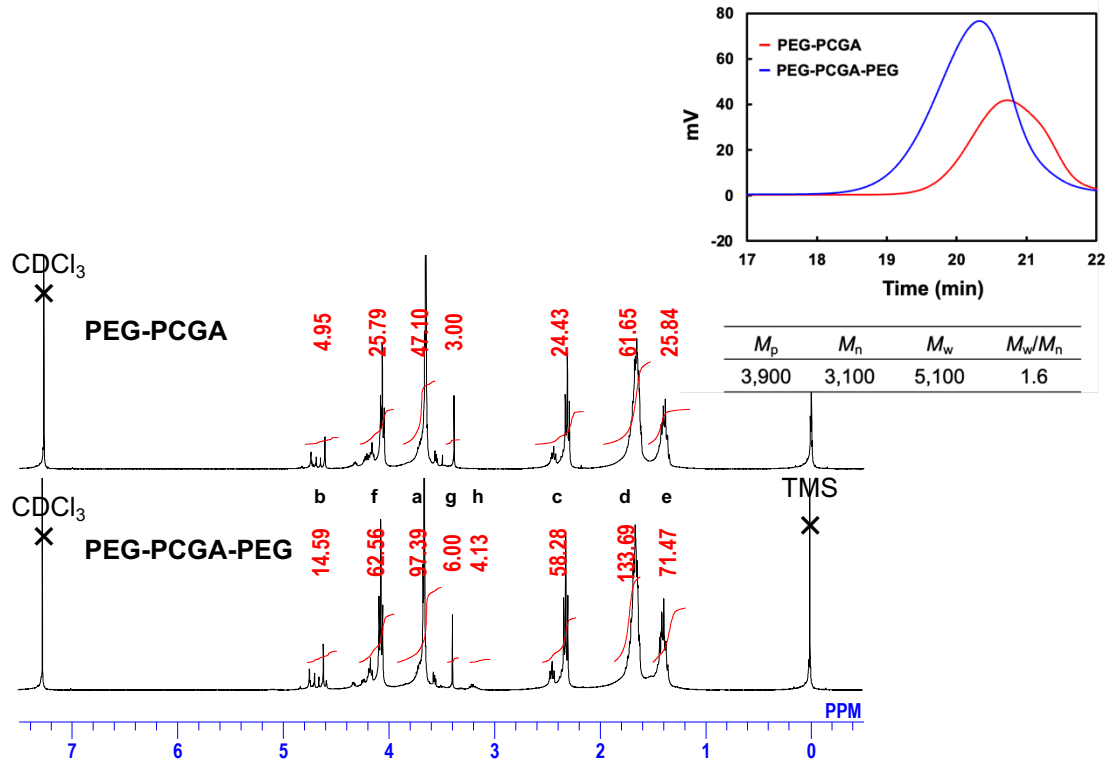


Figure S2(d). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for BAB1.1k-3.7k-4.7.



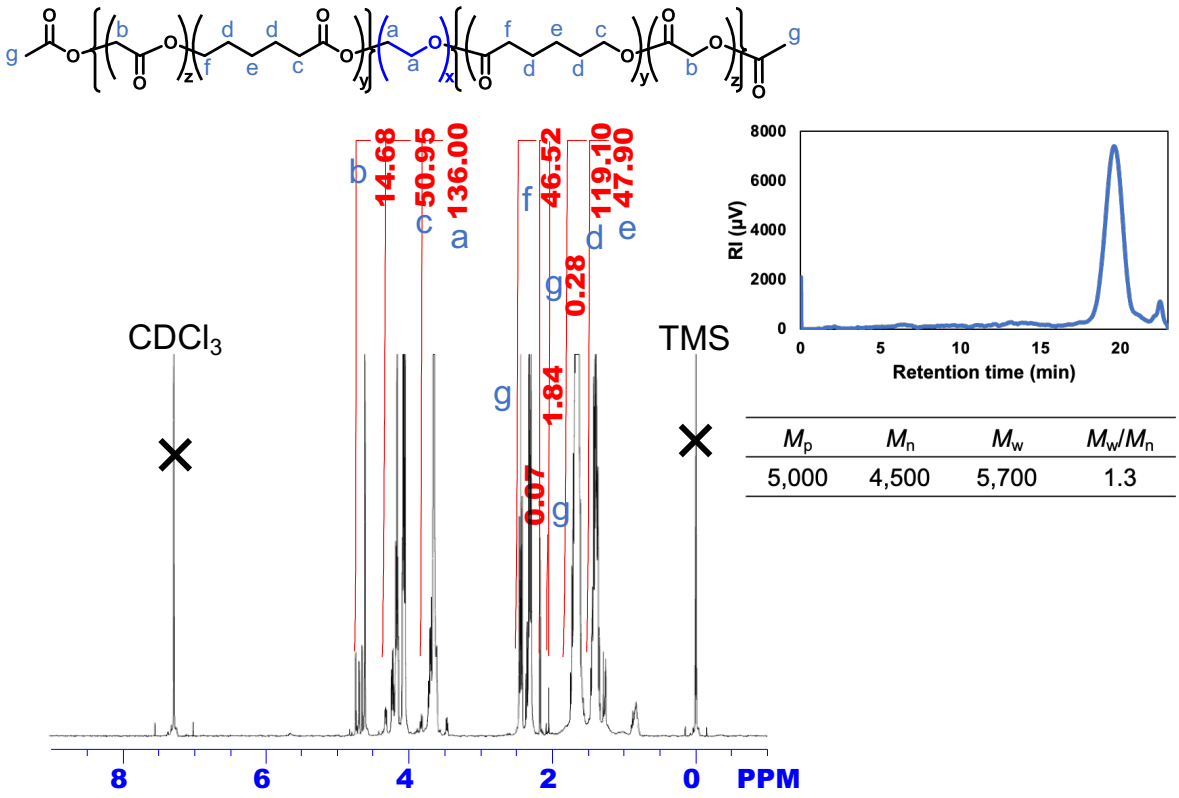
M_p	M_n	M_w	M_w/M_n
4,100	3,600	4,700	1.3

Figure S2(e). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for BAB1.1k-3.8k-3.9.



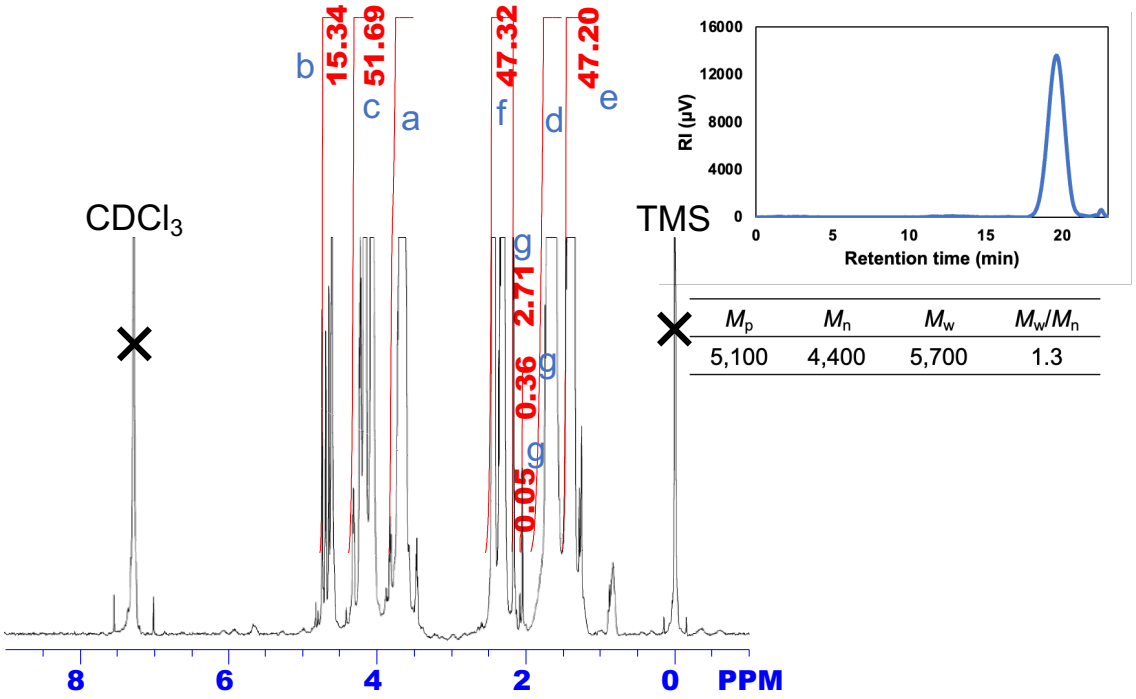
M_p	M_n	M_w	M_w/M_n
3,900	3,100	5,100	1.6

Figure S2(f). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for BAB1.1k-4.3k-3.7.



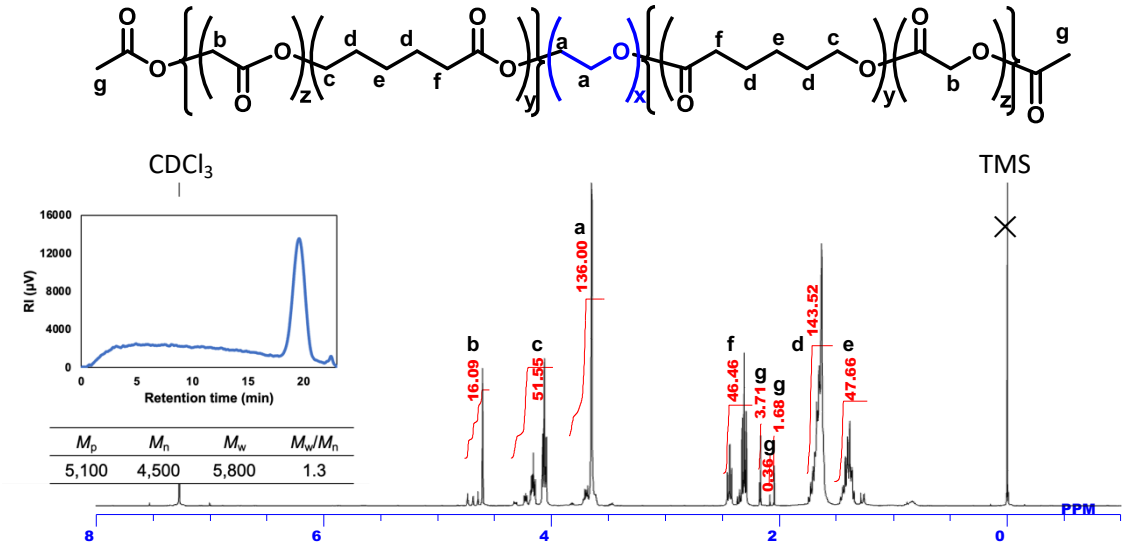
M_p	M_n	M_w	M_w/M_n
5,000	4,500	5,700	1.3

Figure S3(a). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA-Ac_{36}.



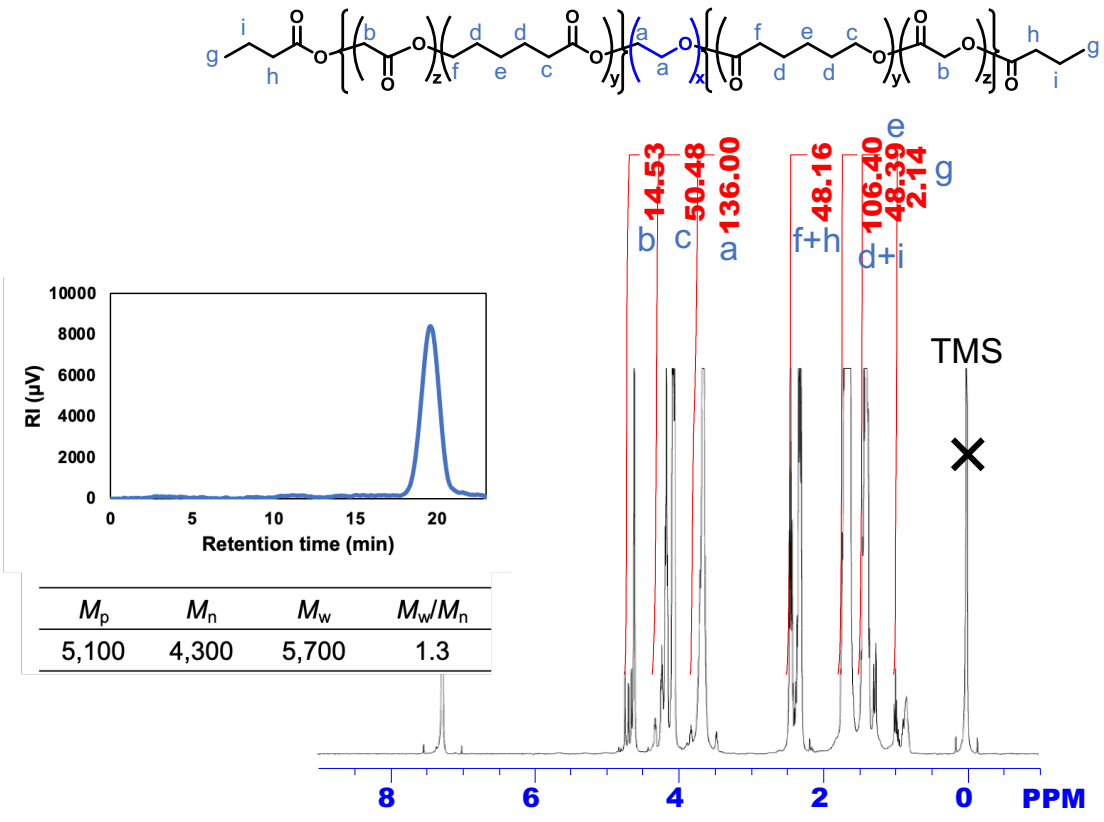
M_p	M_n	M_w	M_w/M_n
5,100	4,400	5,700	1.3

Figure S3(b). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA-Ac_{52}.



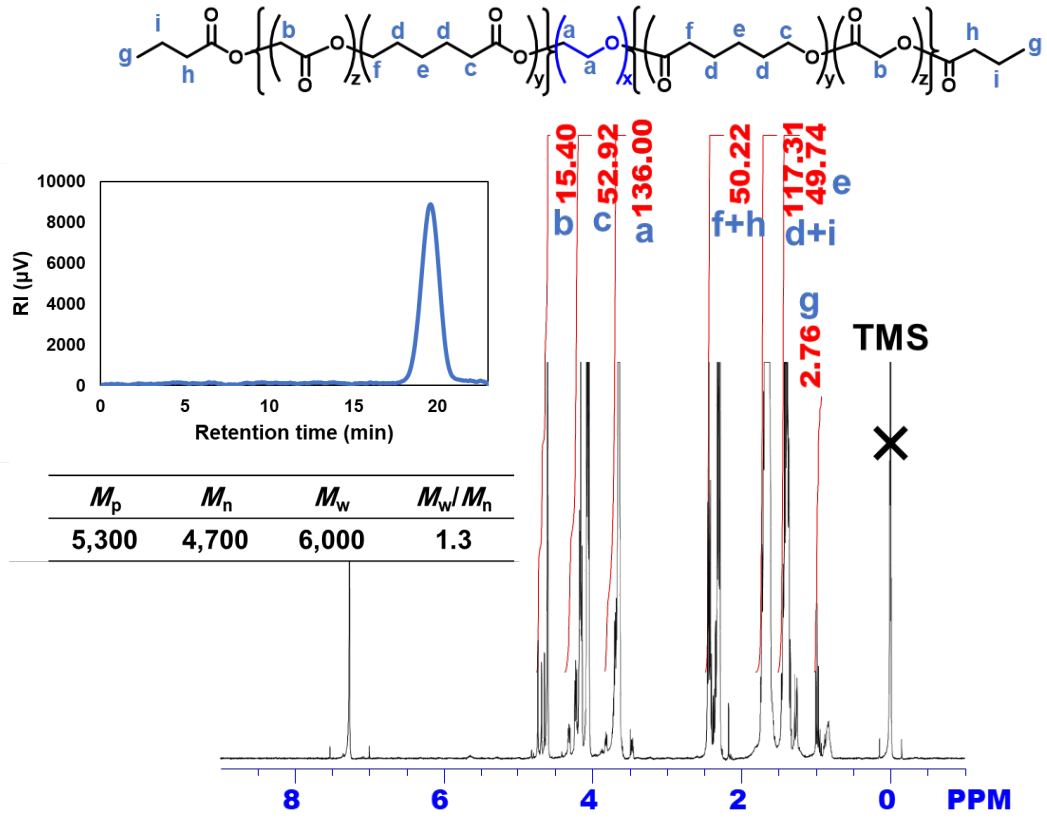
M_p	M_n	M_w	M_w/M_n
5,100	4,500	5,800	1.3

Figure S3(c). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA-Ac_{96}.



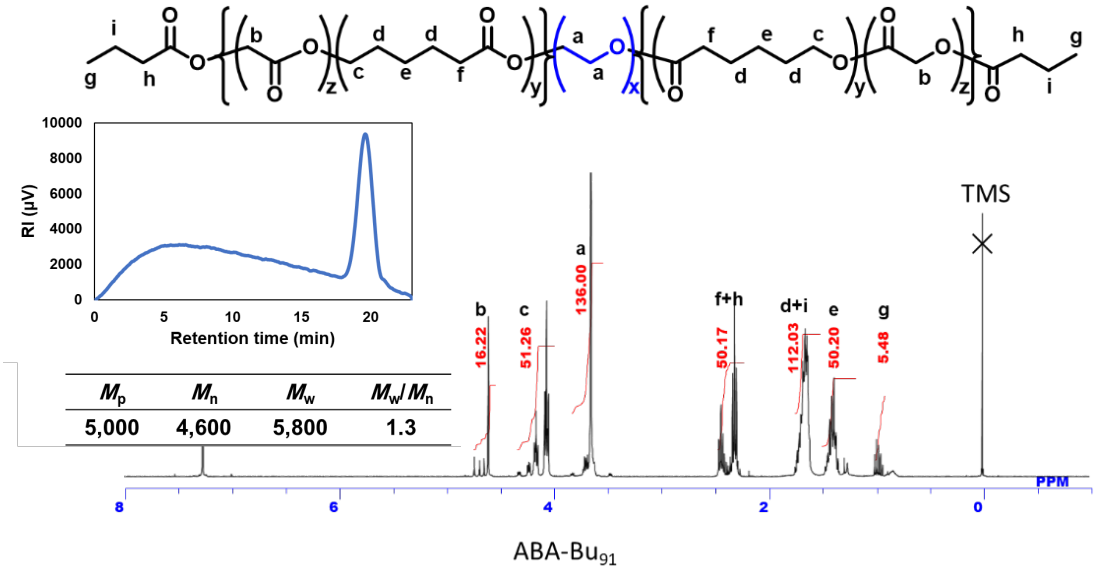
M_p	M_n	M_w	M_w/M_n
5,100	4,300	5,700	1.3

Figure S3(d). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA-Bu_{36}.



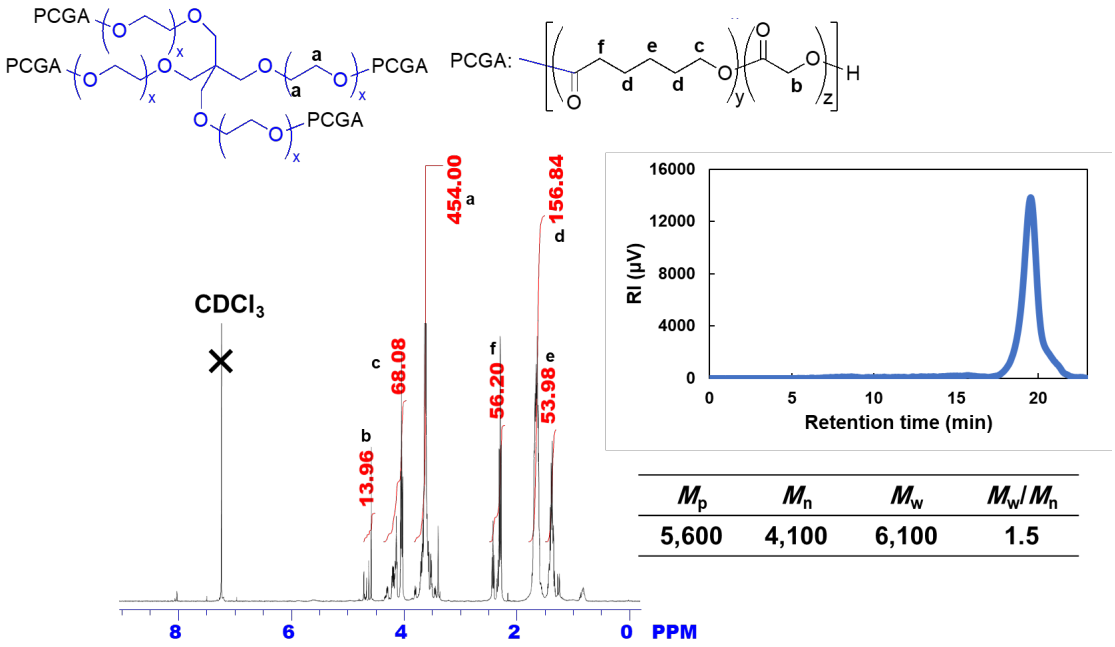
M_p	M_n	M_w	M_w/M_n
5,300	4,700	6,000	1.3

Figure S4(a). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA-Bu_{46}.



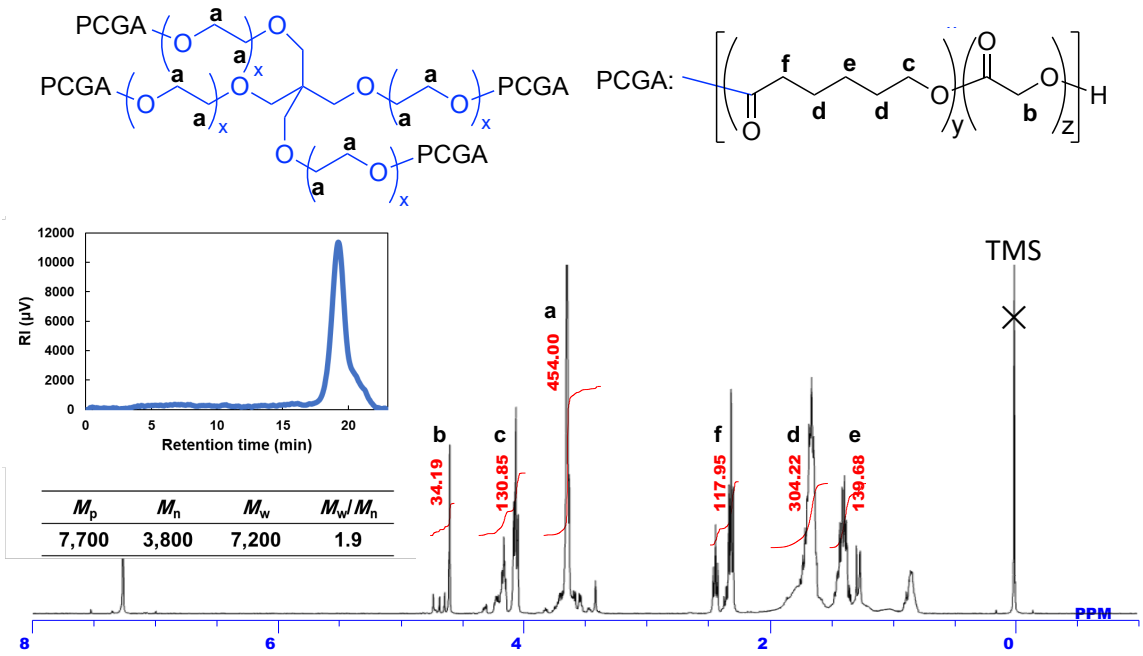
M_p	M_n	M_w	M_w/M_n
5,000	4,600	5,800	1.3

Figure S4(b). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for ABA-Bu_{91}.



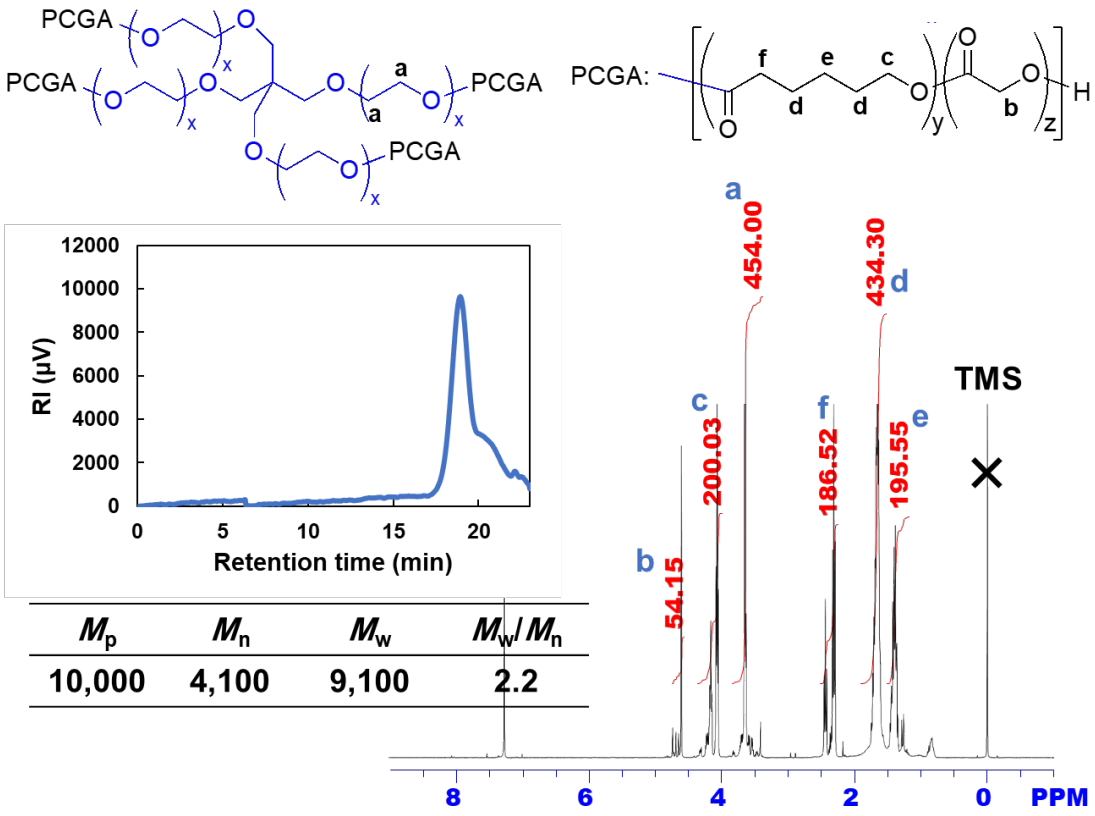
M_p	M_n	M_w	M_w/M_n
5,600	4,100	6,100	1.5

Figure S5(a). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for 4-arm5.0k-3.6k.



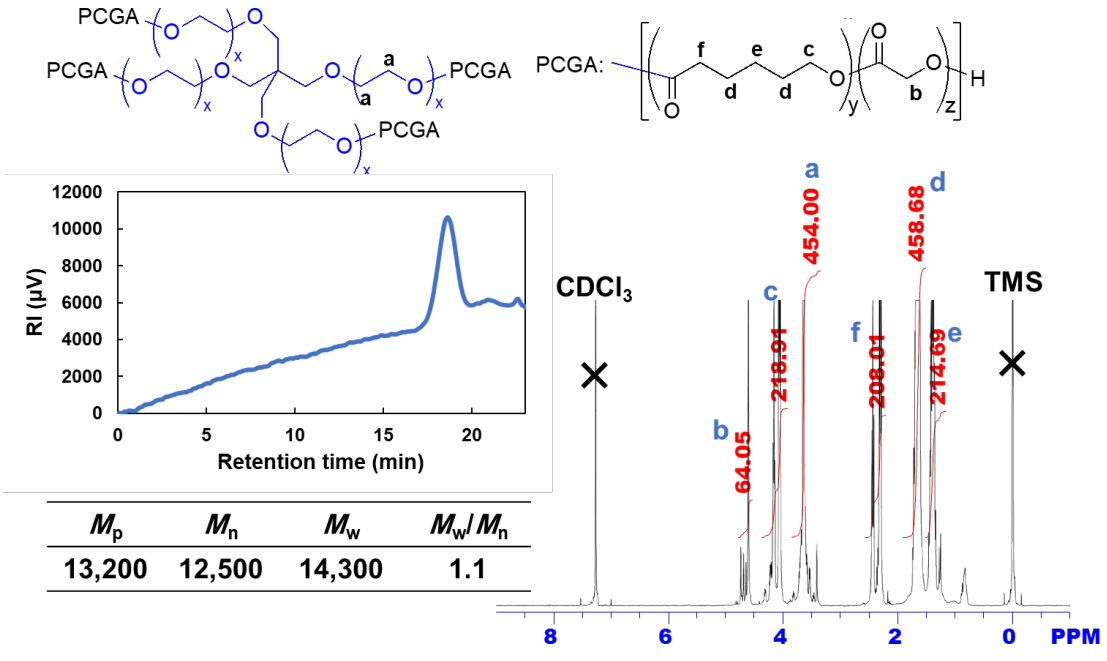
M_p	M_n	M_w	M_w/M_n
7,700	3,800	7,200	1.9

Figure S5(b). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for 4-arm5.0k-7.6k.



M_p	M_n	M_w	M_w/M_n
10,000	4,100	9,100	2.2

Figure S5(c). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for 4-arm5.0k-12.0k.



M_p	M_n	M_w	M_w/M_n
13,200	12,500	14,300	1.1

Figure S5(d). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for 4-arm5.0k-13.6k.

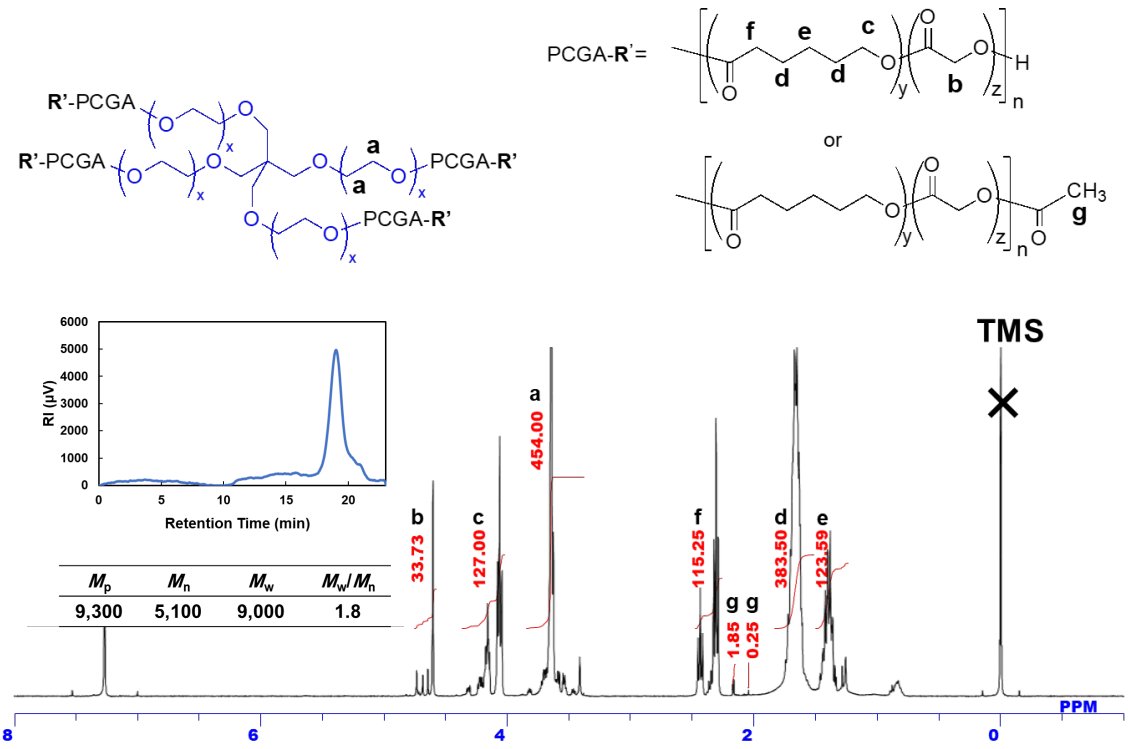


Figure S6(a). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for 4-arm-Ac_{18}.

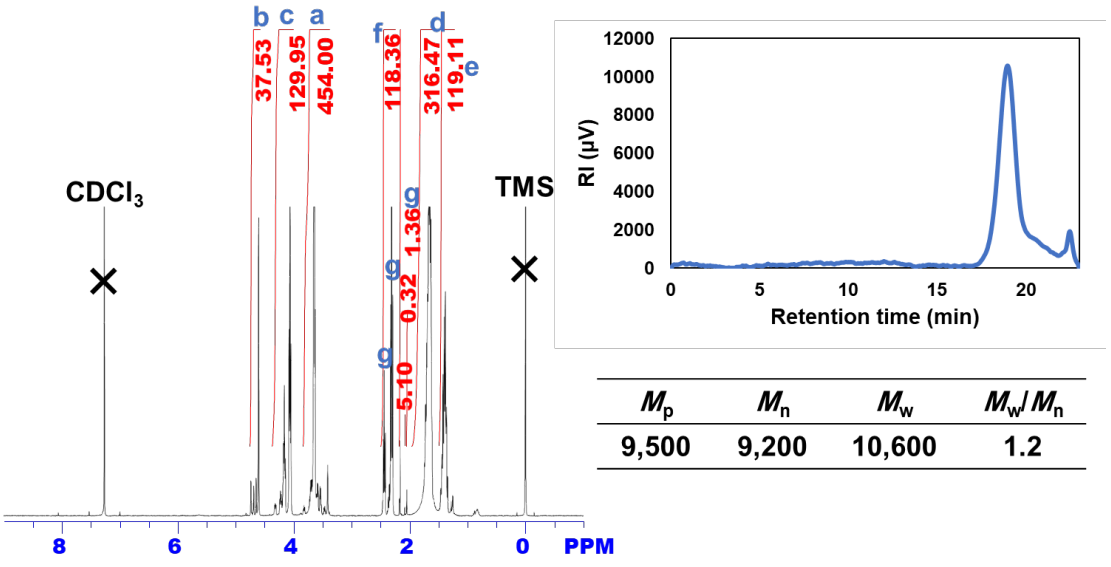


Figure S6(b). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for 4-arm-Ac_{56}.

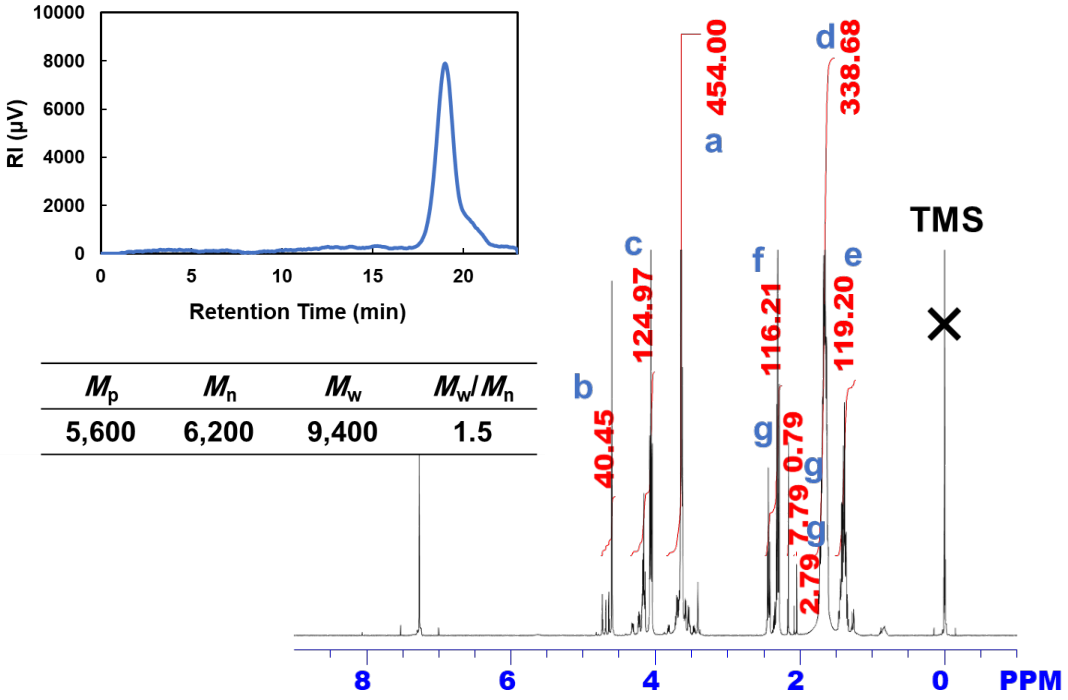


Figure S6(c). ^{1}H-NMR spectrum (in $CDCl_3$) and elution profile of SEC for 4-arm-Ac_{95}.

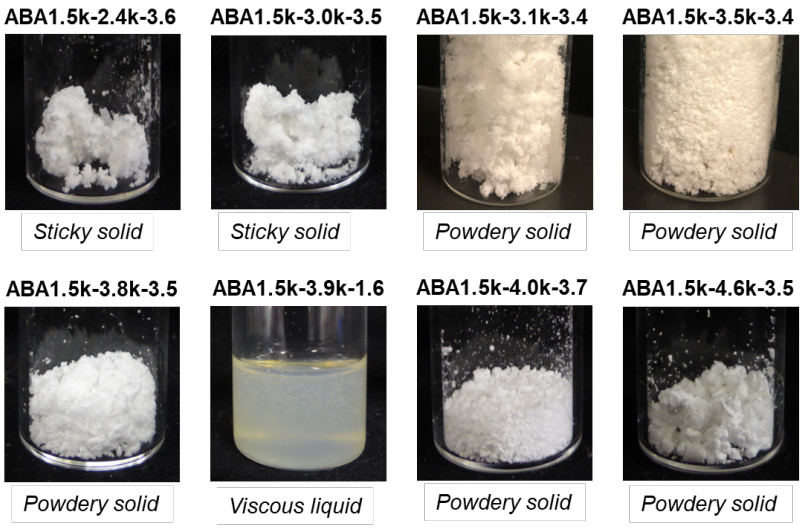


Figure S7. Photographs of PCGA-PEG-PCGA triblock copolymers (ABA1.5k series) synthesized with PEG_{1540}.

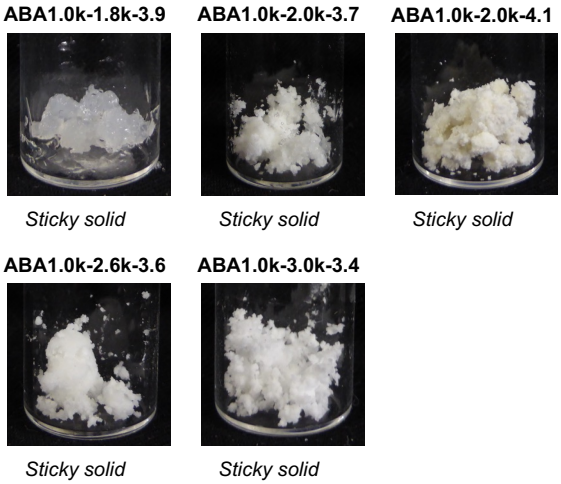


Figure S8. Photographs of PCGA-PEG-PCGA triblock copolymers (ABA1.0k series) synthesized with PEG_{1000}.

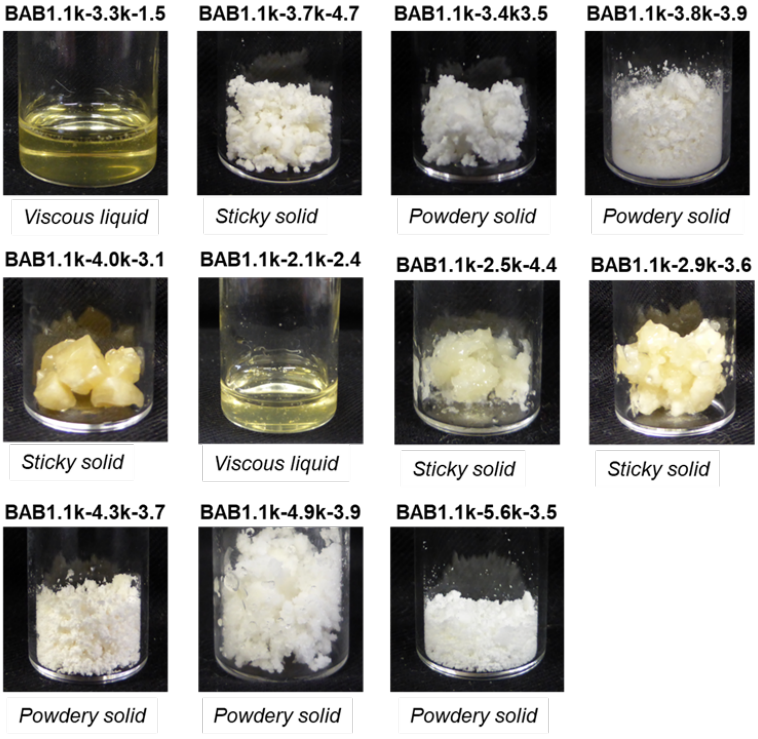


Figure S9. Photographs of PEG-PCGA-PEG triblock copolymers (BAB series) synthesized.

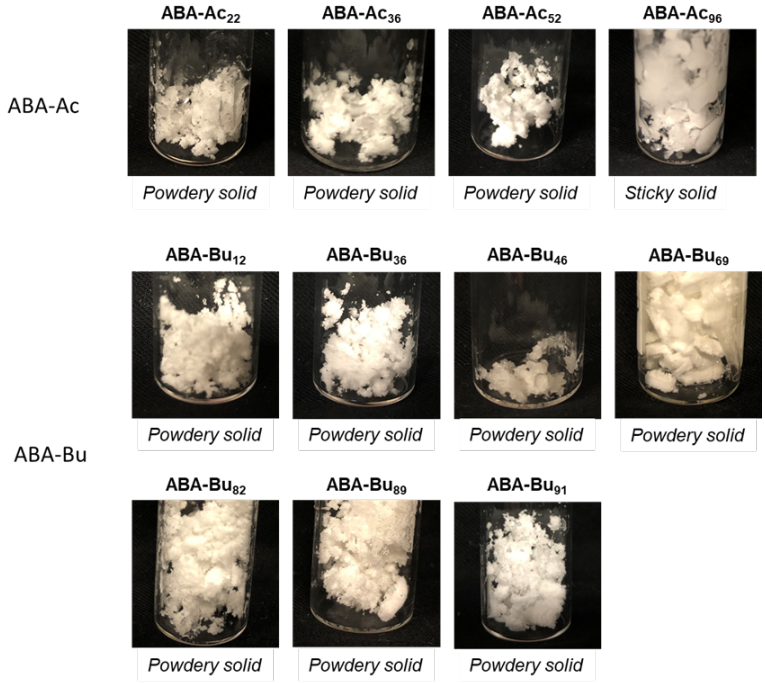


Figure S10. Photographs of partially acetylated or butyrylated PCGA-PEG-PCGA (ABA-Ac series and ABA-Bu series) synthesized.

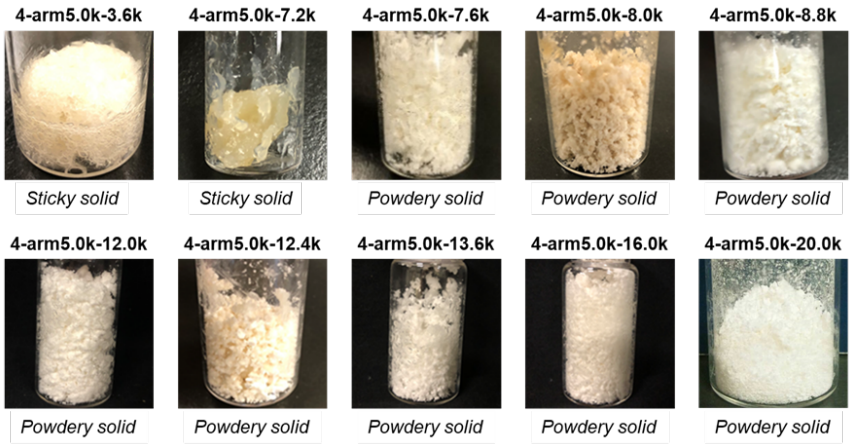


Figure S11. Photographs of 4-arm PEG-PCGA copolymers (4-arm series) synthesized.

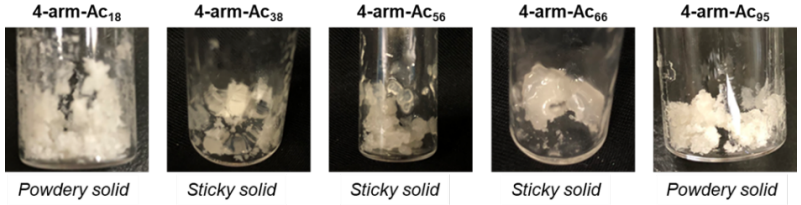


Figure S12. Photographs of partially acetylated 4-arm PEG-PCGA copolymers (4-arm-Ac series) synthesized.

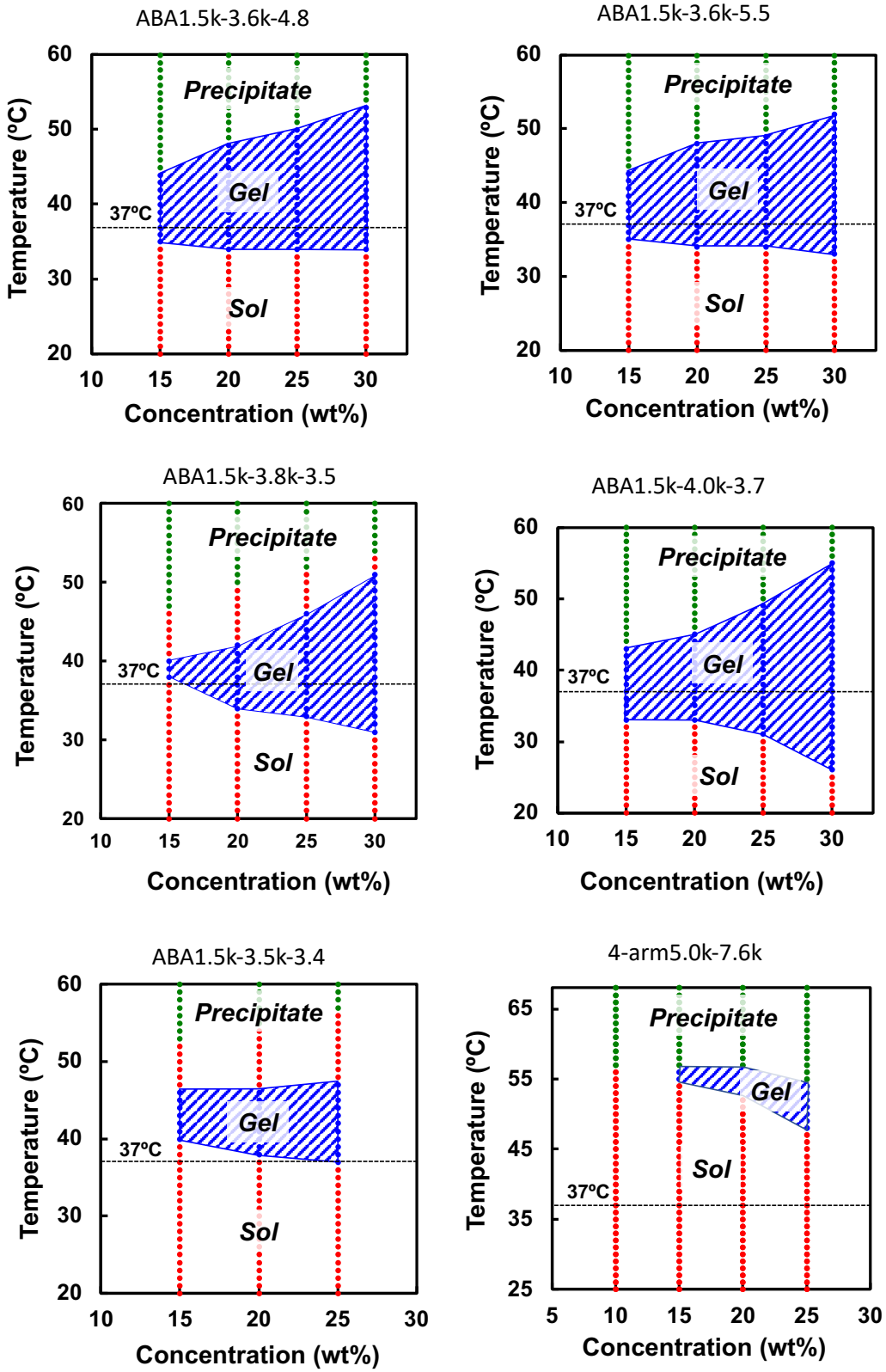
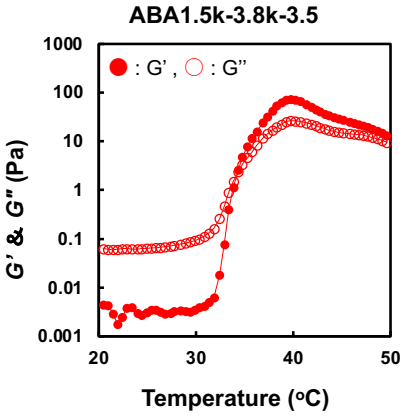
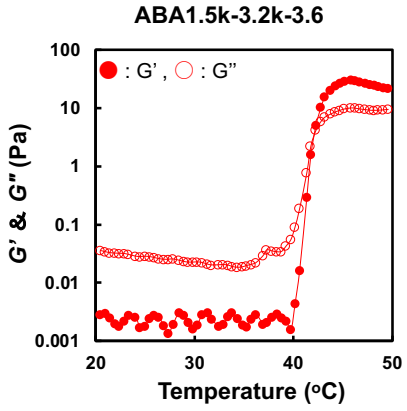


Figure S13. Typical examples of phase diagram in PBS (pH = 7.4).

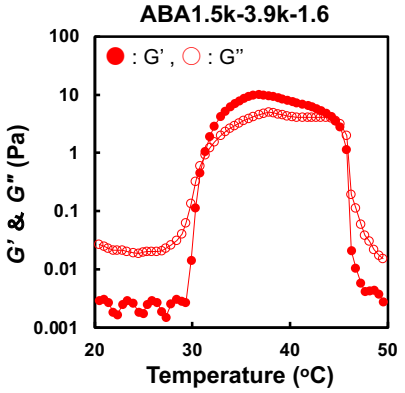
●: Sol; ●: Gel; ●: Precipitate.



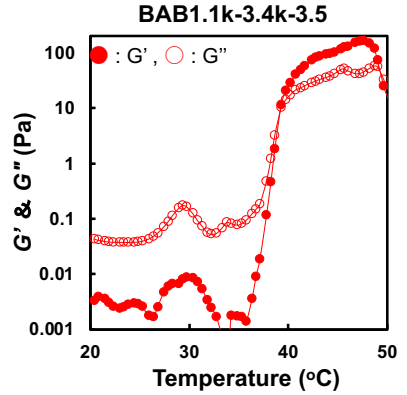
T_{gel} [°C]	G' at 37°C [Pa]	G'max [Pa]	$T_{G',max}$ [°C]
34.3	32.4	74.2	39.7



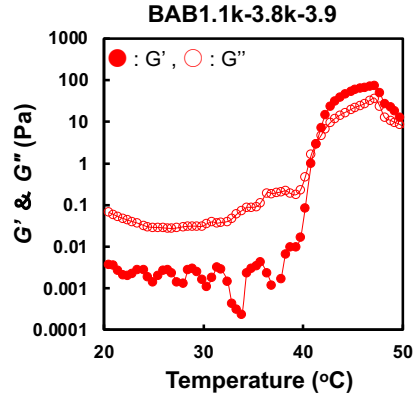
T_{gel} [°C]	G' at 37°C [Pa]	G'max [Pa]	$T_{G',max}$ [°C]
42.3	0.002	30.7	45.8



T_{gel} [°C]	G' at 37°C [Pa]	G'max [Pa]	$T_{G',max}$ [°C]
31.3	10.1	10.1	36.8



T_{gel} [°C]	G' at 37°C [Pa]	G'max [Pa]	$T_{G',max}$ [°C]
39.3	0.02	164.4	47.6



T_{gel} [°C]	G' at 37°C [Pa]	G'max [Pa]	$T_{G',max}$ [°C]
41.8	0.001	74.1	47.2

T_{gel}: Gelation temperature (G' taking over G'')
G'max : Maximum value of G'
$T_{G',max}$: Temperature when G' was maximum

Figure S14. Typical examples of temperature-dependent storage (G', closed symbols) and loss moduli (G'', open symbols) estimated by reoplogical measuremants in PBS (pH = 7.4).

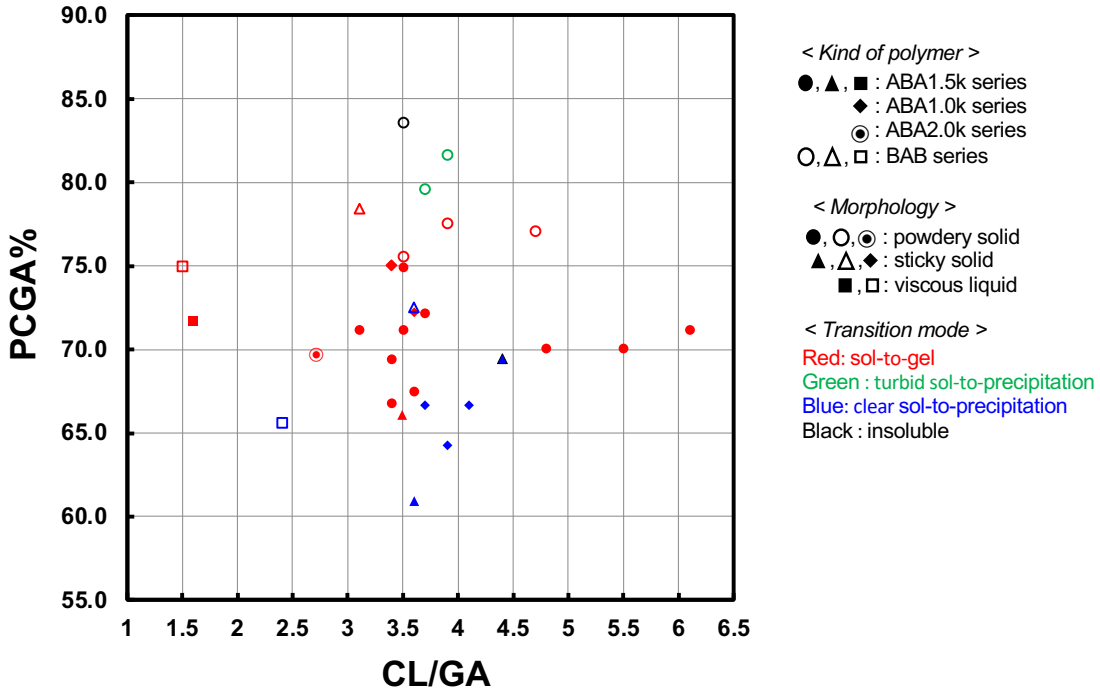


Figure S15. Effects of PCGA segment (PCGA%) content and CL/GA ratios on linear block copolymer morphology and transition modes.

PCGA% = [(MW of total polymer) − (MW of PEG unit)] / (MW of total polymer) × 100 (%)

Closed circle, triangle, and square: ABA1.5k series (MW of PEG = 1540); closed diamond: ABA1.0k series (MW of PEG = 1000); double circle: ABA2.0k; open symbols: BAB series. Circle: powdery solid, triangle and diamond: sticky solid; square: viscous liquid. Red, sol-to-gel; green, turbid sol-to-precipitate; blue, clear sol-to-precipitate; black, insoluble.

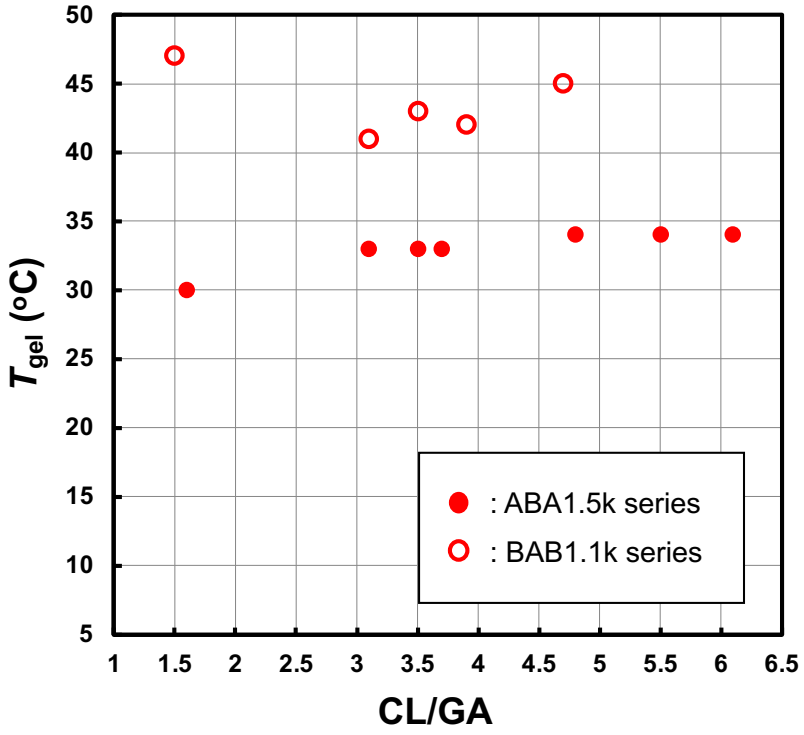


Figure S16. Relationship between gelation temperature (T_{gel}) and molar ration of CL unit to GA unit (CL/GA) for ABA and BAB triblock copolymers with similar MW PCGA segment length. For ABA series, copolymers with MW of PEG = 1.5k and MW of PCGA = 3.6k – 4.0k were shown. For BAB series, copolymers with MW of PCGA = 3.3k – 4.0k were shown. Closed red circle: ABA1.5k series (MW of PEG = 1540), open red circle: BAB series.

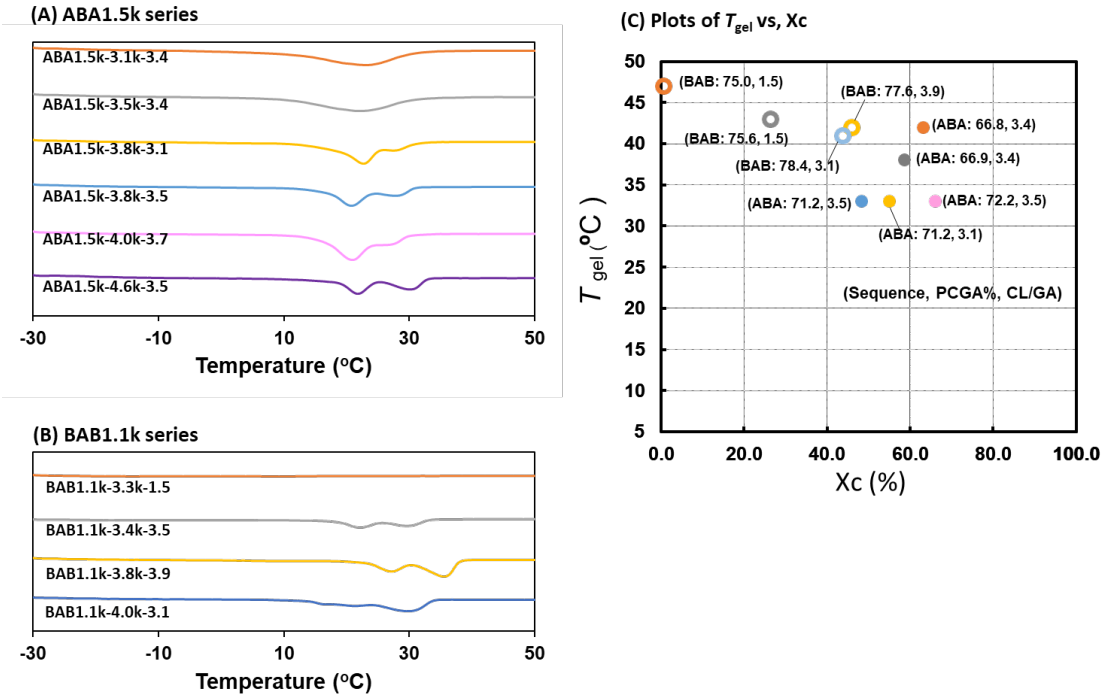


Figure S17. Results of differential scanning calorimetry for (A) ABA1.5k series and (B) BAB1.1k series, and (C) plots of T_{gel} vs. crystallinity (Xc). Closed symbol: ABA series and open symbols: BAB series. For each plot, sequence and PCGA% and CL/GA ratio were indicated in the blackets. The original data were shown in **Table S6**.

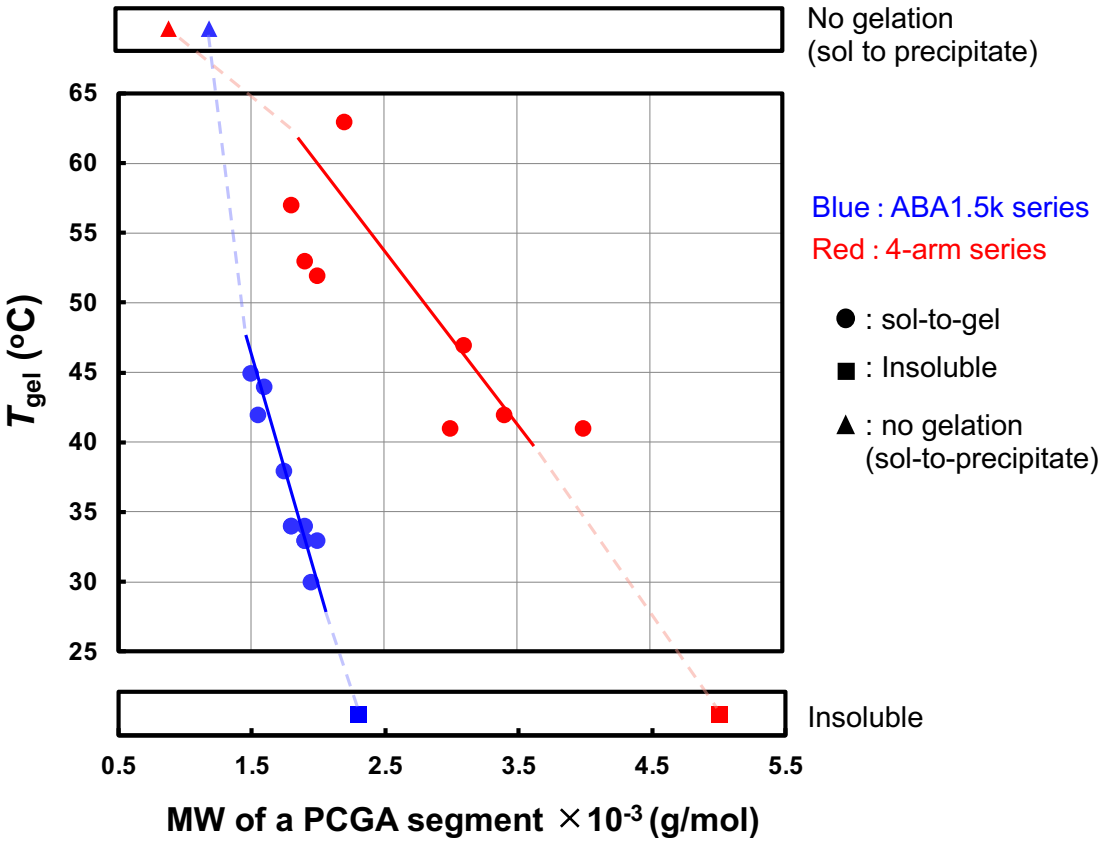


Figure S18. Comparison of the effect of MW of one PCGA segment (g/mol) on the gelation temperature (T_{gel}) for linear ABA triblock (ABA1.5k series) and 4-arm branched PEG-PCGA copolymers (4-arm series).

Circle: sol-to-gel transition, triangle: no gelation (sol-to-precipitate), square: insoluble. Blue: ABA1.5k series (MW of PEG = 1540); red:4-arm series.

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