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Assembled Structures and Chiroptical Properties of Amphiphilic Block Copolymers Synthesized by RAFT Polymerization of *N*-Acryloyl-L-Alanine

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Experimental Part

General Polymerization Procedure. All polymerizations were carried out with AIBN as an initiator in a degassed sealed tube. A representative example for the homopolymerization of A-Ala-OH is as follows: A-Ala-OH (0.286 g, 2.0 mmol), benzyl 1-pyrrolecarbodithioate (4.7 mg, 0.020 mmol), AIBN (1.6 mg, 0.010 mmol), and DMF (1.14 mL) were placed in a dry glass ampule equipped with a magnetic stirring bar, and then the solution was degassed by three freeze-evacuate-thaw cycles. After the ampule was flame-sealed under vacuum, it was stirred at 60 ^{o}C for 24 h. The characteristic yellow color remained during the polymerization. The reaction was stopped by rapid cooling with liquid nitrogen. For the determination of the monomer conversion, the ^{1}H NMR spectrum of the polymerization mixture collected just after the polymerization was measured in DMSO-d_6 at room temperature, and the integration of the monomer C=C-*H* resonance at around 5.6 ppm was compared with the sum of N-C-*H* peak intensity of the polymer and the monomer at around 3.8-4.6 ppm. Conversion determined by this method was 97 %. The polymer obtained was purified by reprecipitation two times from a DMF solution into a large excess of ethyl acetate/hexane (1/1 vol-%), and the resulting product was dried under vacuum at room temperature: yield 0.23 g, 81%. ^{1}H NMR (DMSO-d_6): δ 0.6-2.3 (6H, C*H* and CH_2 in the polymer main chain and >CH-CH_3), 3.8-4.6 (1H, NC*H*COO), 7.0-8.4 (1H, N*H*), and 11.7-13.5 (1H, COO*H*) ppm.

For size-exclusion chromatography (SEC) measurements, the resulting poly(A-Ala-OH)s were directly modified by methylation of the carboxylic acid groups using trimethylsilyldiazomethane according to a method reported previously with a slight modification.[39, 45] In this way, 25 mg of each sample was dissolved in a mixture of THF/methanol (1/1 vol-%, to get solubilization at room temperature), overall volume 2.0 mL. The yellow solution of trimethylsilyldiazomethane (0.50 mL, 1.0 mmol, $(CH_3)_3SiCHN_2$/COOH group in poly(A-Ala-OH) = 85/15 molar ratio) was added dropwise at room temperature into the polymer solution. Upon addition, bubbles appeared and the bright yellow solution became instantaneously pale yellow. After the methylation agent was added completely, the solution was stirred for 1 h more at room temperature. After removing the solvents by evaporation, the methylated samples were employed without any purification for the SEC measurements. For the confirmation of the degree of the esterification, the methylated mixture was precipitated from THF into diethylether, and then sample was evaluated by ^{1}H NMR spectroscopy (see Supporting Information). ^{1}H NMR ($CDCl_3$): δ 0.7-2.7 (6H, C*H* and CH_2 in the polymer main chain and >CH-CH_3), 3.5-4.0 (3H, COOCH_3), 4.0-4.8 (1H, NC*H*COO), and 7.6-8.4 (1H, N*H*) ppm. The ^{1}H NMR spectra of poly(A-Ala-OMe) and poly(A-Ala-OH) are shown in Figure S2 (see Supporting Information).

For the kinetic study, typically a mixed solution of the A-Ala-OH, benzyl 1-pyrrolecarbodithioate, AIBN, and DMF were divided into 5-7 ampules, and then each solution was degassed by three freeze-evacuate-thaw cycles. After the ampule was sealed by flame under vacuum, it was stirred at 60 ^{o}C for the desired time. The reaction was stopped by rapid cooling with liquid nitrogen, and the monomer conversion was determined by the ^{1}H NMR spectrum of the polymerization mixture. The crude poly(A-Ala-OH)s were modified by the methylation, and the resulting poly(A-Ala-OMe)s were used directly for

SEC measurements without any purification.

Synthesis of Block Copolymer Using Polystyrene as Macro-CTA. The synthesis of a block copolymer composed of styrene and A-Ala-OH was conducted using polystyrene macro-CTA as follows: styrene (2.02 g, 20 mmol), benzyl 1-pyrrolecarbodithioate (46.7 mg, 0.20 mmol), AIBN (6.6 mg, 0.040 mmol), and toluene (2.0 mL) were placed in a dry ampule, followed by degassing and stirring at 60 ^{o}C for 24 h. After the product was purified by precipitation into methanol, the resulting polystyrene (M_n = 5900, M_w/M_n = 1.26) was employed as a macro-CTA.

The dithiocarbamate-terminated polystyrene (0.24 g, 0.04 mmol), AIBN (3.3 mg, 0.02 mmol), A-Ala-OH (0.14 g, 1.0 mmol), and DMF (1.52 mL) were placed in a dry ampule. After the solution was degassed by three freeze-evacuate-thaw cycles, the polymerization was conducted at 60 ^{o}C for 48 h (conversion determined by ^{1}H NMR spectroscopy = 90%). The reaction mixture was purified by two times reprecipitation from a DMF solution into a mixture of ethyl acetate and hexane (1/1 vol-%) and isolated by filtration, to give a block copolymer, polystyrene-*b*-poly(A-Ala-OH). The comonomer composition was determined using ^{1}H NMR spectroscopy by a comparison of the peak at 3.9-4.7 ppm attributed the methine proton (NC*H*COO, 1H) of the A-Ala-OH unit and peaks at 6.2-7.3 ppm correspond to the aromatic protons (5H) of the styrene unit. The methylation of poly(A-Ala-OH) segment in the block copolymer was also conducted by treating the carboxylic acid groups using trimethylsilyldiazomethane to afford polystyrene-*b*-poly(A-Ala-OMe), which was employed for SEC measurement (M_n = 9100, M_w/M_n = 1.26, which corresponds to M_n = 8800 in the carboxylic acid form).

Synthesis of Block Copolymer Using Poly(A-Phe-OMe) as Macro-CTA. Poly(A-Phe-OMe) employed as a macro-CTA was prepared using benzyl 1-pyrrolecarbodithioate as a CTA and AIBN as an initiator. A representative example is as follows: A-Phe-OMe (2.00 g, 8.6 mmol), benzyl 1-pyrrolecarbodithioate (68.0 mg, 0.29 mmol), AIBN (23.0 mg, 0.14 mmol), and 1,4-dioxane (6.0 mL) were placed in an ampule, and then the solution was degassed by three freeze-evacuate-thaw cycles. The reaction mixture was stirred at 60 °C for 3.5 h. The poly(A-Phe-OMe) had an M_n (as determined by SEC) of 4700 and a polydispersity index of 1.25 with 82% conversion. The product was purified by precipitation into diethyl ether, and then isolated by filtration. Finally, the resulting poly(A-Phe-OMe) was dried under vacuum at room temperature.

A representative example of the synthesis of the block copolymer using poly(A-Phe-OMe) macro-CTA is as follows: the dithiocarbamate-terminated poly(A-Phe-OMe) (0.282 g, 0.06 mmol; M_n = 4700, M_w/M_n = 1.25), AIBN (4.9 mg, 0.03 mmol), A-Ala-OH (0.26 g, 1.8 mmol), and DMF (2.1 mL) were placed in a dry ampule. After the solution was degassed by three freeze-evacuate-thaw cycles, the polymerization was conducted at 60 °C for 48 h. Conversion of the double bonds, as detected by ^{1}H NMR, was > 99%. The reaction mixture was precipitated two times from DMF into in a large excess of mixture of ethyl acetate and hexane (1/1 vol-%) and isolated by filtration. The copolymer composition was determined using ^{1}H NMR spectroscopy by a comparison of peaks associated with the two comonomers. The peak at 3.9-4.8 ppm is attributed the methine proton (NC*H*COO, 1H) of the A-Ala-OH and A-Phe-OMe units, whereas the peak at 6.9-7.4 ppm correspond to the aromatic protons (5H) of the A-Phe-OMe unit. Poly(A-Phe-OMe)-*b*-poly(A-Ala-OMe), obtained by the methylation had an M_n (as determined by SEC) of 11400 and a polydispersity index of 1.19 , which corresponds to M_n = 11000 in the carboxylic acid form.

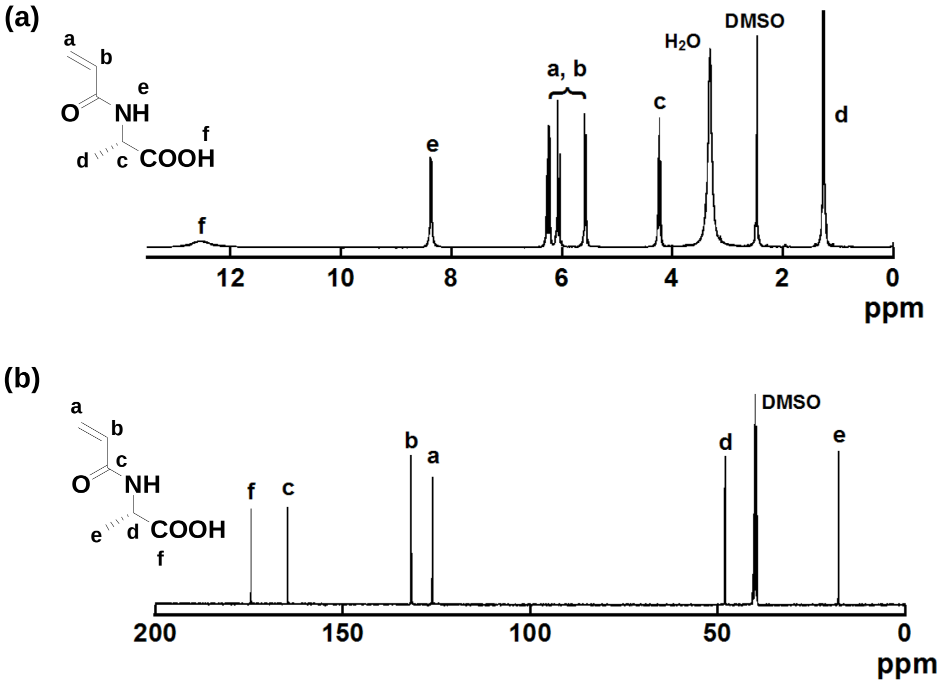

Figure S1. (a) ^{1}H and (b) ^{13}C NMR spectra of A-Ala-OH (d_6-DMSO).

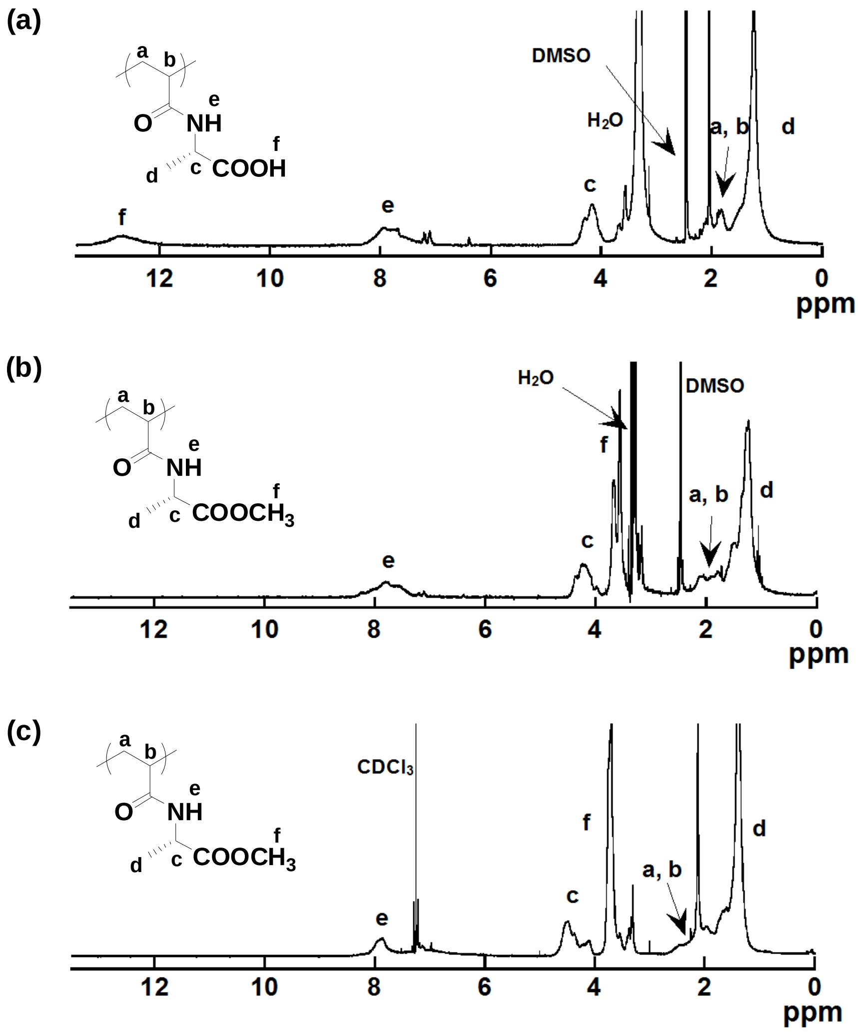

Figure S2. ^{1}H NMR spectra (d_6-DMSO) of (a) poly(A-Ala-OH) prepared by RAFT polymerization, and poly(A-Ala-OMe) (b; d_6-DMSO, c; $CDCl_3$) obtained by methylation of the corresponding poly(A-Ala-OH).

Table S1. Polymerization of *N*-Acryloyl-L-alanine (A-Ala-OH) Using Different Chain Transfer Agents (CTAs) in MeOH at 60 °C for 24 h[a)]

entry	CTA[b)]	conv.[c)] %	M_n [d)] (theory)	M_n [e)] (SEC)	M_w/M_n [e)] (SEC)
1	—	>99	—	109000	3.36
2	CTA 1	11	1100	—	—
3	CTA 2	94	7600	8800	1.25
4	CTA 3	>99	8100	8200	1.34

[a)] $[AIBN]_0/[CTA]_0/[A\text{-}Ala\text{-}OH]_0$ = 1/2/100, monomer conc.= 0.25 g/mL. [b)] CTA 1 = benzyl dithiobenzoate, CTA 2 = benzyl 1-pyrrolecarbodithioate, CTA 3 = *O*-ethyl-*S*-(1-phenylethyl)dithiocabonate. [c)] Calculated by ^{1}H NMR in DMSO-d_6. [d)] The theoretical molecular weight ($M_{n,theory}$) = (MW of A-Ala-OMe) × $[A\text{-}Ala\text{-}OH]_0/[CTA]_0$ × conv. + (MW of CTA), A-Ala-OMe = *N*-acryloyl-L-alanine methyl ester. [e)] Methylated samples were measured by SEC using polystyrene standards in DMF, (10 mM LiBr).

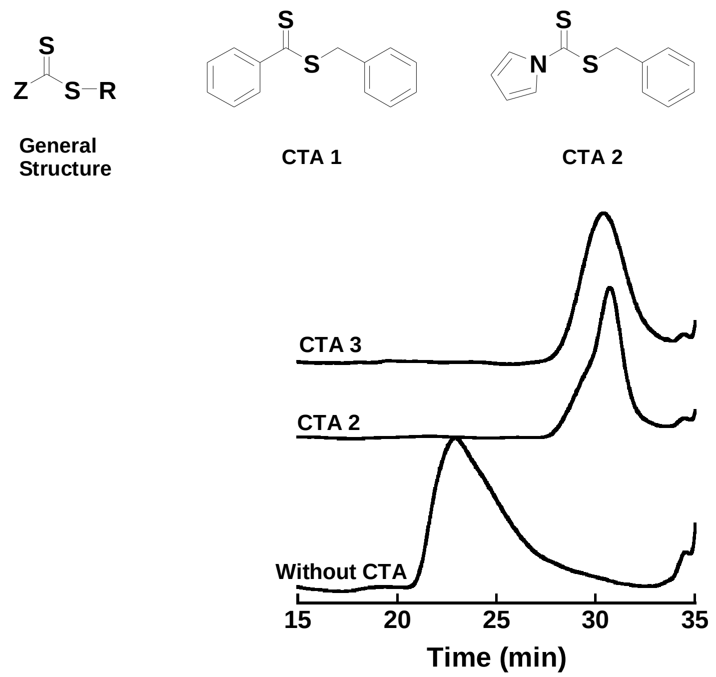

Figure S3. SEC traces of the methylated poly(A-Ala-OH)s obtained by RAFT polymerization using different CTAs.

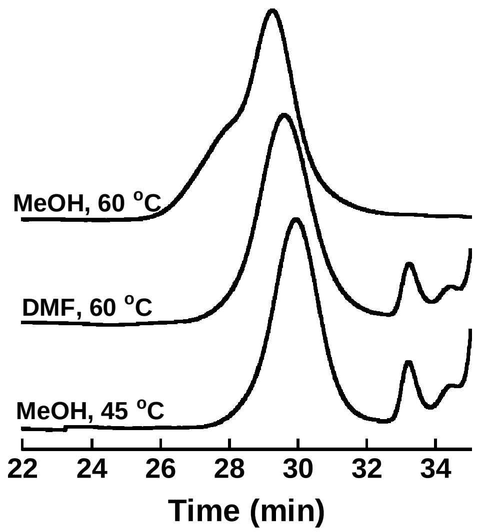

Figure S4 SEC traces of the methylated poly(A-Ala-OH)s obtained by RAFT polymerization of A-Ala-OH at $[\text{A-Ala-OH}]_0/[\text{CTA}]_0/[\text{AIBN}]_0$ = 200/2/1 under different conditions, at where AIBN = 2,2'-azobis(isobutyronitrile), A-Ala-OH = *N*-acryloyl-L-alanine, CTA = benzyl 1-pyrrolecarbodithioate. See Table 1 for detailed polymerization conditions.

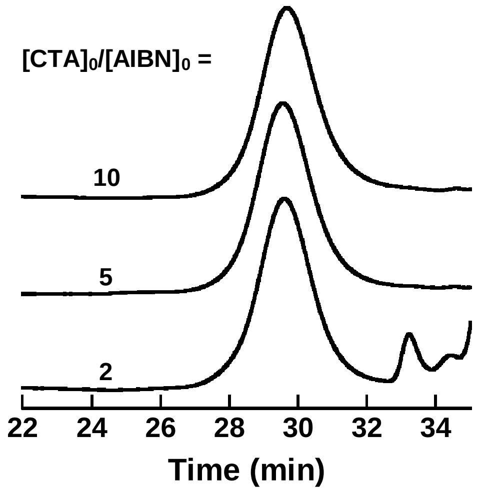

Figure S5. SEC traces of the methylated poly(A-Ala-OH)s obtained by RAFT polymerization of A-Ala-OH at different $[CTA]_0/[AIBN]_0$ ratios, keeping the monomer-to-chain transfer agent ratio at a constant value of $[A\text{-}Ala\text{-}OH]_0/[CTA]_0$ = 100/1 in DMF. See Table 1 for detailed polymerization conditions.

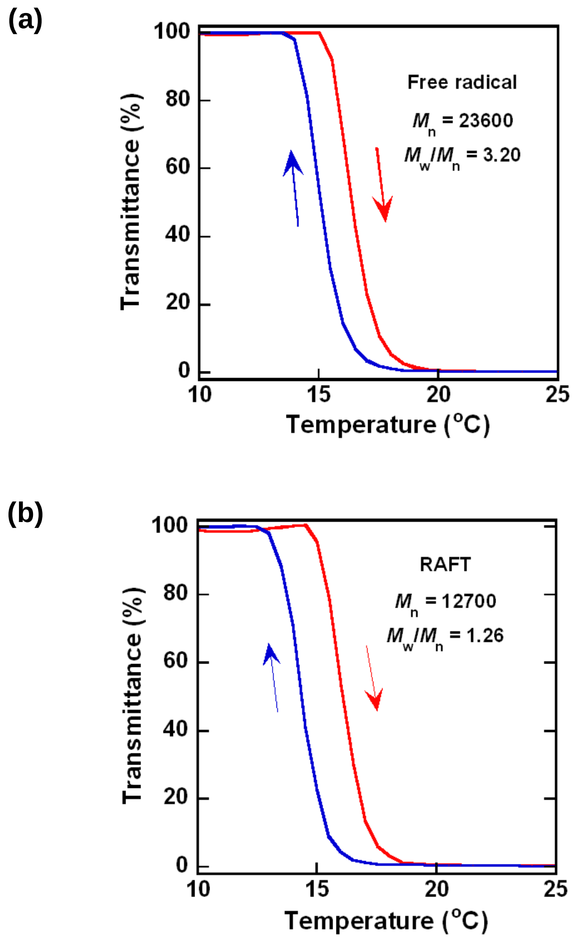

Figure S6. Temperature dependence of the transmittance at 500 nm of aqueous solution (2.0 g/L) of the poly(A-Ala-OMe)s prepared by (a) free radical and (b) RAFT polymerizations of A-Ala-OH, followed by the methylation.