Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supplementary Information

Biocompatible poly(N-(ω-acryloyloxy-n-alkyl)-2-pyrrolidone)s with widely-tunable lower critical solution temperatures (LCSTs): a promising alternative to poly(N-isopropylacrylamide)

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Experimental Procedures

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Materials

Solvents of special grade were used unless otherwise specified. 4-Aminobutanol, 5-aminopentanol, 6-aminohexanol, *N*-(2-hydroxyethyl)-2-pyrrolidone (NHEtP), *N*-(3-hydroxypropyl)-2-pyrrolidone (NHPrP), γ-butyrolactone, 2-pyrrolidone, acryloyl chloride, triethylamine, and 2,2'-azobis(isobutyronitrile) (AIBN) were purchased from Tokyo Chemical Industries Co., Ltd. (Japan). Dichloromethane, toluene, dimethylformamide (DMF), diethyl ether, methanol, and 12 M hydrochloric acid were purchased from Kanto Chemicals Co., Inc. (Japan). Paraformaldehyde, potassium hydroxide, potassium carbonate anhydrous, urea, lithium bromide, sodium chloride, and magnesium sulfate anhydrous were purchased from FUJIFILM Wako Pure Chemical Co., Ltd. (Japan). Chloroform-*d* was purchased from Merck/Sigma-Aldrich (Germany). AIBN was purified by recrystallization from methanol prior to use.

Measurements

The ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were acquired using an AVANCE III (Bulker Daltonics Inc., USA) spectrometer (400 MHz) at 25 °C. The values of number-average molecular weight (M_n) and polydispersity index ($Đ$) of the synthesized polymers were determined by size exclusion chromatography (SEC) on an HPLC system (Prominence; Shimadzu Co., Japan) equipped with a refractive index (RI) detector using DMF (10 mM LiBr) as an eluent (flow rate 1.0 mL/min, temperature: 40 °C, column: TSKgel ALPHA-M (Tosoh Co., Japan)). Poly(methyl methacrylate) (PMMA) was purchased from Agilent Technologies Ltd. (USA) and used as the calibration standard. The differential scanning calorimetry (DSC) measurements were performed on a X-DSC7000

(Seiko Instruments Inc., Japan). The samples for DSC measurements under wet condition were prepared according to our previous reports.[S1]

Synthesis Procedure

Synthesis of *N*-hydroxymethyl-2-pyrrolidone (NHMeP)

2-Pyrrolidinone 106.2 g (1.25 mol) and potassium hydroxide 0.3 g (5.34 mmol) were mixed and heated at 80 °C. Paraformaldehyde 37.8 g (1.25 mol as formaldehyde) was added to the mixture and stirred for 30 min at 80 °C. After reaction, the mixture was cooled to ambient temperature and added toluene 200 mL to precipitate the resultant molecule. The precipitation was collected and further purified twice from toluene to give the pure *N*-hydroxymethyl-2-pyrrolidone (NHMeP) as a white solid (77.2 g, 53.6%).

^{1}H NMR [400 MHz, chloroform-*d*, tetramethylsilane (TMS)] (Figure S1A): δ = 2.05 ppm (-NCH$_2$C*H*$_2$CH$_2$C(=O)-), *quin*, 2H, Hz), 2.39 ppm (-NCH$_2$CH$_2$C*H*$_2$C(=O)-, *t*, 2H, Hz), 3.58 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O)-, *t*, 2H, Hz), 4.78 ppm (-NCH$_2$CH$_2$CH$_2$C(=O)-, *s*, 2H, Hz), 5.09 ppm (-CH$_2$O*H*, *s*, 1H, Hz). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S1B): δ = 18.03 ppm (-NCH$_2$*C*H$_2$CH$_2$C(=O)-), 31.56 ppm (-NCH$_2$CH$_2$*C*H$_2$C(=O)-), 46.27 ppm (-N*C*H$_2$CH$_2$CH$_2$C(=O)-), 66.43 ppm (-*C*H$_2$OH), 176.28 ppm (-NCH$_2$CH$_2$CH$_2$*C*(=O)-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 116.0633, $[M+H]^+_{obs.}$ = 116.0699.

$EA_{obs.}$ ($EA_{calc.}$): H; 7.84% (7.88%), C; 52.30% (52.16%), N; 12.17% (12.17%).

Synthesis of *N*-(4-hydroxybutyl)-2-pyrrolidone (NHBuP)

4-Aminobutanol 75.0 g (0.84 mol) and γ-butyrolactone 72.4 g (0.84 mol) was mixed and stirred at ambient temperature for 1 h. The resultant mixture was transferred to autoclave and stirred at 250 °C for 8 h. The objective molecule was collected by distillation (169-171 °C, 3 mmHg) to obtained the pure *N*-(4-hydroxybutyl)-2-pyrrolidone (NHBuP) as a colorless liquid (90.0 g, 70.7%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S2A): δ = 1.54 ppm (-CH$_2$C*H*$_2$CH$_2$CH$_2$OH, *quin*, 2H), 1.60 ppm (-CH$_2$CH$_2$C*H*$_2$CH$_2$OH-, *quin*, 2H), 2.02 ppm (-NCH$_2$C*H*$_2$CH$_2$C(=O)-, *quin*, 2H), 2.37 ppm (-NCH$_2$CH$_2$C*H*$_2$C(=O)-, *t*, 2H), 2.95 ppm (-CH$_2$CH$_2$CH$_2$CH$_2$O*H*, *s*, 1H), 3.31 ppm (-C*H*$_2$CH$_2$CH$_2$CH$_2$OH, *t*, 2H), 3.39 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O)-, *t*, 2H), 3.64 ppm (-CH$_2$CH$_2$CH$_2$C*H*$_2$OH, *t*, 2H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S2B): δ = 18.03 ppm (-NCH$_2$C*H*$_2$CH$_2$C(=O)-), 23.96 ppm (-CH$_2$CH$_2$C*H*$_2$CH$_2$OH), 29.66 ppm (-CH$_2$*C*H$_2$CH$_2$CH$_2$OH), 31.08 ppm (-NCH$_2$CH$_2$*C*H$_2$C(=O)-), 42.47 ppm (-*C*H$_2$CH$_2$CH$_2$CH$_2$OH), 47.45 ppm (-N*C*H$_2$CH$_2$CH$_2$C(=O)-), 61.92 ppm (-CH$_2$CH$_2$CH$_2$*C*H$_2$OH), 175.4 ppm (-N(CH$_2$CH$_2$CH$_2$*C*(=O)-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 158.1103, $[M+H]^+_{obs.}$ = 158.1158.

$EA_{obs.}$ ($EA_{calc.}$): H; 9.57% (9.67%), C; 61.13% (61.12%), N; 8.90% (8.91%).

Synthesis of *N*-(5-hydroxypentyl)-2-pyrrolidone (NHPnP)

This molecule was synthesized by the same method with NHBuP.

b.p.: 192-194 °C (3 mmHg).

Yield: 101.3 g (70.4%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S3A): δ = 1.38 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *quin*, 2H), 1.59 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *m*, 4H), 2.02 ppm (-$NCH_2CH_2CH_2C(=O)$-, *quin*, 2H), 2.09 ppm (-$N(CH_2CH_2CH_2CH_2CH_2OH)CH_2CH_2CH_2C(=O)$-, *s*, 2H), 2.39 ppm (-$NCH_2CH_2CH_2C(=O)$-, *t*, 2H), 3.29 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *t*, 2H), 3.39 ppm (-$NCH_2CH_2CH_2C(=O)$-, *t*, 2H), 3.63 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *t*, 2H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S3B): δ = 18.16 ppm (-$NCH_2CH_2CH_2C(=O)$-), 22.99 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 27.35 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 31.46 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 32.68 ppm (-$NCH_2CH_2CH_2C(=O)$-), 42.85 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 47.20 ppm (-$NCH_2CH_2CH_2C(=O)$-), 62.94 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 175.25 ppm (-$NCH_2CH_2CH_2C(=O)$-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 172.1259, $[M+H]^+_{obs.}$ = 172.1308.

$EA_{obs.}$ ($EA_{calc.}$): H; 9.93% (10.01%), C; 63.24% (63.13%), N; 8.16% (8.18%).

Synthesis of *N*-(6-hydroxyhexyl)-2-pyrrolidone (NHHxP)

This molecule was synthesized by the same method with NHBuP.

b.p.: 211-213 °C (3 mmHg).

Yield: 119.3 g (64.4%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S4A): δ = 1.32 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *quin*, 2H), 1.42 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *quin*, 2H), 1.55 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *m*, 4H), 1.90 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *s*, 1H), 2.03 ppm (-$NCH_2CH_2CH_2C(=O)$-, *quin*, 2H), 2.39 ppm (-$NCH_2CH_2CH_2C(=O)$-, *t*, 2H), 3.30 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, *t*, 2H), 3.38 ppm (-$NCH_2CH_2CH_2C(=O)$-, *t*, 2H), 3.63 ppm (-$NCH_2CH_2CH_2C(=O)$-, *t*, 2H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S4B): δ = 17.94 ppm (-$NCH_2CH_2CH_2C(=O)$-), 25.15 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 26.30 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$, 27.15 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 31.31 ppm (-$NCH_2CH_2CH_2C(=O)$-), 32.74 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 42.47 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$-), 47.21 ppm (-$NCH_2CH_2CH_2C(=O)$-), 62.64 ppm (-$CH_2CH_2CH_2CH_2CH_2CH_2OH$), 175.10 ppm (-$NCH_2CH_2CH_2C(=O)$-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 186.1416, $[M+H]^+_{obs.}$ = 186.1464.

$EA_{obs.}$ ($EA_{calc.}$): H; 10.24% (10.34%), C; 64.91% (64.83%), N; 7.54% (7.56%).

Synthesis of *N*-acryloyloxymethyl-2-pyrrolidone (NAMeP)

NHMeP 6.22 g (54.0 mmol) and triethylamine 6.01 g (59.4 mmol) was dissolved to dichloromethane 200 mL and cooled under ice bath. Acryloyl chloride 4.89 g (54.0 mmol) was dissolved to dichloromethane 90 mL and added dropwise to the mixture, and then the solution stirred at ambient temperature for 12 h. The resultant mixture was washed with 1 M HCl_{aq} 100 mL × 3, 5% K_2CO_{3aq} 100 mL × 3, and sat. $NaCl_{aq}$ × 1. The organic layer was collected and dried over $MgSO_4$ anhydrous, and then the solvent was removed *in vacuo* to give a crude. The objective molecule was collected by distillation (76-78 °C, 0.5 mmHg) in the presence of BMH (Seiko Chemical Co., Ltd.) as a polymerization inhibitor for high temperature to obtain the pure *N*-acryloyloxymethyl-2-

pyrrolidone (NAMeP) as a colorless liquid (6.75 g, 73.5%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S5A): δ = 2.05 ppm (-NCH$_2$C*H*$_2$CH$_2$C(=O)-, *quin*, 2H), 2.39 ppm (-NCH$_2$CH$_2$C*H*$_2$C(=O)-, *t*, 2H), 3.57 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O)-, *t*, 2H), 5.44 ppm (-C*H*$_2$OC(=O)CHCH$_a$H$_b$, s, 2H), 5.89 ppm (-CH$_2$OC(=O)CHC*H*$_a$H$_b$, *d*, 1H), 6.14 ppm (-CH$_2$OC(=O)C*H*CH$_a$H$_b$, *dd*, 1H), 6.48 ppm (-CH$_2$OC(=O)CHCH$_a$*H*$_b$, *d*, 1H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S5B): δ = 17.91 ppm (-NCH$_2$*C*H$_2$CH$_2$C(=O)-), 30.68 ppm (-NCH$_2$CH$_2$*C*H$_2$C(=O)-), 46.70 ppm (-N*C*H$_2$CH$_2$CH$_2$C(=O)-), 65.52 ppm (-*C*H$_2$OC(=O)CHCH$_a$H$_b$), 127.88 ppm (-CH$_2$OC(=O)CH*C*H$_a$H$_b$), 131.94 ppm (-CH$_2$OC(=O)*C*HCH$_a$H$_b$), 165.89 ppm (-CH$_2$O*C*(=O)CHCH$_a$H$_b$), 176.20 ppm (-NCH$_2$CH$_2$CH$_2$*C*(=O)-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 170.0739, $[M+H]^+_{obs.}$ = 170.0739.

$EA_{obs.}$ ($EA_{calc.}$): H; 6.53% (6.55%), C; 56.64% (56.80%), N; 8.17% (8.28%).

Synthesis of *N*-(2-acryloyloxyethyl)-2-pyrrolidone

This molecule was synthesized by the same method with NAMeP.

b.p.: 83-85 °C (0.5 mmHg).

Yield: 7.64 g (77.3%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S6A): δ = 2.04 ppm (-NCH$_2$C*H*$_2$CH$_2$C(=O)-, *quin*, 2H), 2.39 ppm (-NCH$_2$CH$_2$C*H*$_2$C(=O)-, *t*, 2H), 3.47 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O)-, *t*, 2H), 3.59 ppm (-C*H*$_2$CH$_2$OC(=O)CHCH$_a$H$_b$, *t*, 2H), 4.31 ppm (-CH$_2$C*H*$_2$OC(=O)CHCH$_a$H$_b$, *t*, 2H), 5.88 ppm (-CH$_2$CH$_2$OC(=O)CHC*H*$_a$H$_b$, *d*, 1H), 6.11 ppm (-CH$_2$CH$_2$OC(=O)C*H*CH$_a$H$_b$, *dd*, 1H), 6.41 ppm (-CH$_2$CH$_2$OC(=O)CHCH$_a$*H*$_b$), *d*, 1H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S6B): δ = 18.27 ppm (-NCH$_2$*C*H$_2$CH$_2$C(=O)-), 30.84 ppm (-NCH$_2$CH$_2$*C*H$_2$C(=O)-), 41.76 ppm (-*C*H$_2$CH$_2$OC(=O)CHCH$_a$H$_b$, 48.16 ppm (-*C*H$_2$CH$_2$OC(=O)CHCH$_a$H$_b$), 62.16 ppm (-CH$_2$*C*H$_2$OC(=O)CHCH$_a$H$_b$), 128.12 ppm (-CH$_2$CH$_2$OC(=O)*C*HCH$_a$H$_b$), 131.44 ppm (-CH$_2$CH$_2$OC(=O)CH*C*H$_a$H$_b$), 166.08 ppm (-CH$_2$CH$_2$O*C*(=O)CHCH$_a$H$_b$), 175.33 ppm (-NCH$_2$CH$_2$CH$_2$*C*(=O)-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 184.0895, $[M+H]^+_{obs.}$ = 184.0995.

$EA_{obs.}$ ($EA_{calc.}$): H; 7.04% (7.15%), C; 58.96% (59.00%), N; 7.67% (7.65%).

Synthesis of *N*-(3-acryloyloxypropyl)-2-pyrrolidone

This molecule was synthesized by the same method with NAMeP.

b.p.: 94-96 °C (0.5 mmHg).

Yield: 7.98 g (74.9%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S7A): δ = 1.92 ppm (-CH$_2$C*H*$_2$CH$_2$OC(=O)CHCH$_a$H$_b$, *quin*, 2H), 2.04 ppm (-NCH$_2$C*H*$_2$CH$_2$C(=O)-, *quin*, 2H), 2.37 ppm (-NCH$_2$CH$_2$C*H*$_2$C(=O)-, *t*, 2H), 3.39 ppm (-N(C*H*$_2$CH$_2$CH$_2$OC(=O)CHCH$_a$H$_b$)C*H*$_2$CH$_2$CH$_2$C(=O)-, *m*, 4H), 4.18 ppm (-CH$_2$CH$_2$C*H*$_2$OC(=O)CHCH$_a$H$_b$, *t*, 2H), 5.83 ppm (-CH$_2$CH$_2$CH$_2$OC(=O)CHC*H*$_a$H$_b$, *d*, 1H), 6.14 ppm (-CH$_2$CH$_2$CH$_2$OC(=O)C*H*CH$_a$H$_b$, *dd*, 1H), 6.41 ppm (-CH$_2$CH$_2$CH$_2$OC(=O)CHCH$_a$*H*$_b$, *d*, 1H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S7B): δ = 17.79 ppm (-NCH$_2$*C*H$_2$CH$_2$C(=O)-), 26.81 ppm (-CH$_2$*C*H$_2$CH$_2$OC(=O)CHCH$_a$H$_b$), 31.08 ppm (-NCH$_2$CH$_2$*C*H$_2$C(=O)-), 39.62 ppm (-

C$H_2CH_2CH_2OC(=O)CHCH_aH_b$), 47.21 ppm (-N*C*$H_2CH_2CH_2C(=O)$-), 62.16 ppm (-$CH_2CH_2$*C*$H_2OC(=O)CHCH_aH_b$), 128.36 ppm (-$CH_2CH_2CH_2OC(=O)$*C*$HCH_aH_b$), 130.96 ppm (-$CH_2CH_2CH_2OC(=O)CH$*C*$H_aH_b$), 166.32 ppm (-$CH_2CH_2CH_2O$*C*$(=O)CHCH_aH_b$), 175.09 ppm (-$NCH_2CH_2CH_2$*C*(=O)-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 198.1052, $[M+H]^+_{obs.}$ = 198.1079.

$EA_{obs.}$ ($EA_{calc.}$): H; 7.59% (7.67%), C; 60.88% (60.90%), N; 7.05% (7.10%).

Synthesis of *N*-(4-acryloyloxybutyl)-2-pyrrolidone

This molecule was synthesized by the same method with NAMeP.

b.p.: 104-106 °C (0.5 mmHg).

Yield: 9.24 g (80.6%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S8A): δ = 1.63 ppm (-CH_2*C*H_2*C*$H_2CH_2OC(=O)CHCH_aH_b$, *m*, 4H), 1.69 ppm (-NCH_2*C*$H_2CH_2C(=O)$-, *quin*, 2H), 2.43 ppm (-NCH_2*C*$H_2CH_2C(=O)$-, *t*, 2H), 3.33 ppm (-*C*$H_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *t*, 2H), 3.40 ppm (-N*C*$H_2CH_2CH_2C(=O)$-, *t*, 2H), 4.19 ppm (-$CH_2CH_2CH_2$*C*$H_2OC(=O)CHCH_aH_b$, *t*, 2H), 5.83 ppm (-$CH_2CH_2CH_2CH_2OC(=O)CHC$*H*$_aH_b$, *d*, 1H), 6.14 ppm (-$CH_2CH_2CH_2CH_2OC(=O)C$*H*$CH_aH_b$, *dd*, 1H), 6.45 ppm (-$CH_2CH_2CH_2CH_2OC(=O)CHCH_a$*H*$_b$, *d*, 1H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S8B): δ = 17.79 ppm (-NCH_2*C*$H_2CH_2C(=O)$-), 23.96 ppm (-CH_2CH_2*C*$H_2CH_2OC(=O)CHCH_aH_b$), 26.09 ppm (-CH_2*C*$H_2CH_2CH_2OC(=O)CHCH_aH_b$)-), 31.56 ppm (-$NCH_2CH_2$*C*$H_2C(=O)$-), 42.47 ppm (-*C*$H_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 47.21 ppm (-N*C*$H_2CH_2CH_2C(=O)$-), 64.30 ppm (-$CH_2CH_2CH_2$*C*$H_2OC(=O)CHCH_aH_b$), 128.83 ppm (-$CH_2CH_2CH_2CH_2OC(=O)$*C*$HCH_aH_b$-), 130.97 ppm (-$CH_2CH_2CH_2CH_2OC(=O)CH$*C*$H_aH_b$), 166.32 ppm (-$CH_2CH_2CH_2CH_2O$*C*$(=O)CHCH_aH_b$), 175.09 ppm (-$NCH_2CH_2CH_2$*C*(=O)-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 211.1208, $[M+H]^+_{obs.}$ = 212.1287.

$EA_{obs.}$ ($EA_{calc.}$): H; 8.02% (8.11%), C; 62.53% (62.54%), N; 6.63% (6.63%).

Synthesis of *N*-(5-acryloyloxypentyl)-2-pyrrolidone

This molecule was synthesized by the same method with NAMeP.

b.p.: 111-113 °C (0.5 mmHg).

Yield: 9.21 g (75.6%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S9A): δ = 1.39 ppm (-CH_2CH_2*C*$H_2CH_2CH_2OC(=O)CHCH_aH_b$, *quin*, 2H), 1.57 ppm (-CH_2*C*$H_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *quin*, 2H), 1.69 ppm (-$CH_2CH_2CH_2$*C*$H_2CH_2OC(=O)CHCH_aH_b$, *quin*, 2H), 2.04 ppm (-NCH_2*C*$H_2CH_2C(=O)$-, *quin*, 2H), 2.39 ppm (-NCH_2CH_2*C*$H_2C(=O)$-, *t*, 2H), 3.28 ppm (-N*C*$H_2CH_2CH_2C(=O)$-, *t*, 2H), 3.41 ppm (-*C*$H_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *t*, 2H), 4.14 ppm (-$CH_2CH_2CH_2CH_2$*C*$H_2OC(=O)CHCH_aH_b$, *t*, 2H), 5.86 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHC$*H*$_aH_b$, *d*, 1H), 6.14 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)C$*H*$CH_aH_b$, *dd*, 1H), 6.41 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_a$*H*$_b$, *d*, 1H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S9B): δ = 18.27 ppm (-NCH_2*C*$H_2CH_2C(=O)$-), 23.25 ppm ((CH_2CH_2*C*$H_2CH_2CH_2OC(=O)CHCH_aH_b$), 26.81 ppm (-$CH_2CH_2CH_2$*C*$H_2CH_2OC(=O)CHCH_aH_b$), 28.47 ppm (-

$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 31.08 ppm (-$NCH_2CH_2CH_2C(=O)$-), 42.47 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 46.98 ppm (-$NCH_2CH_2CH_2C(=O)$-), 64.30 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 128.36 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 130.97 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 166.32 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 175.10 ppm (-$NCH_2CH_2CH_2C(=O)$-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 226.1365, $[M+H]^+_{obs.}$ = 226.1445.

$EA_{obs.}$ ($EA_{calc.}$): H; 8.34% (8.50%), C; 63.91% (63.98%), N; 6.19% (6.22%).

Synthesis of *N*-(6-acryloyloxyhexyl)-2-pyrrolidone

This molecule was synthesized by the same method with NAMeP.

b.p.: 121-123 °C (0.5 mmHg).

Yield: 10.25 g (79.0%).

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S10A): δ = 1.34 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *m*, 4H), 1.53 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *quin*, 2H), 1.68 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *quin*, 2H), 2.02 ppm (-$NCH_2CH_2CH_2C(=O)$-, *quin*, 2H), 2.38 ppm (-$NCH_2CH_2CH_2C(=O)$-, *t*, 2H), 3.28 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *t*, 2H), 3.38 ppm (-$NCH_2CH_2CH_2C(=O)$-, *t*, 2H), 4.14 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *t*, 2H), 5.82 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *d*, 1H), 6.12 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *dd*, 1H), 6.41 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$, *d*, 1H). ^{13}C NMR [75 MHz, chloroform-*d*, TMS] (Figure S10B): δ = 18.01 ppm (-$NCH_2CH_2CH_2C(=O)$-), 25.68 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 26.45 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 27.23 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 28.49 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 31.06 ppm (-$NCH_2CH_2CH_2C(=O)$-), 42.37 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 47.10 ppm (-$NCH_2CH_2CH_2C(=O)$-), 64.52 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 128.62 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 130.55 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 166.22 ppm (-$CH_2CH_2CH_2CH_2CH_2OC(=O)CHCH_aH_b$), 174.79 ppm (-$NCH_2CH_2CH_2C(=O)$-).

HRMS (FAB MASS, m/z): $[M+H]^+_{theo.}$ = 240.1512, $[M+H]^+_{obs.}$ = 240.1583.

$EA_{obs.}$ ($EA_{calc.}$): H; 8.84% (8.85%), C; 65.28% (65.25%), N; 5.84% (5.85%).

General Method for Synthesis of PNARPs by Radical Polymerization

In a typical synthesis of PNARPs, NARPs (20 mmol) and AIBN (1/200 equiv.) were dissolved in DMF. The solutions were poured into a two-neck flask at a constant monomer concentration of 2 M, and deoxygenated by bubbling dry Ar for 30 min. Then, the reaction mixtures were placed in a preheated oil bath at 60 °C. After polymerization for 40 min, the mixtures were cooled to room temperature and poured into a large excess of diethyl ether to precipitate PNARPs. The resultant polymers were further purified by reprecipitation method from the acetone/diethyl ether system. The solvents were removed in *vacuo* to obtain the pure polymers as a

white solid (PNAMeP) or colorless viscous liquid (PNAEtP, PNAPrP, PNABuP, PNAPnP, and PNAHxP). The chemical structure of the polymers was characterized by ^{1}H NMR spectroscopy. The values of M_n and $Đ$ were estimated from SEC analysis. The T_gs were determined by DSC measurement.

^{1}H NMR [400 MHz, chloroform-*d*, TMS]: **PNAMeP** (Figure S11): δ = 1.38-2.57 ppm (methylene of main chain, 2H; methine of main chain, 1H; -NCH$_2$C*H*$_2$CH$_2$C(=O), 2H; -NCH$_2$CH$_2$C*H*$_2$C(=O), 2H), 3.48-3.65 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O), 2H), 5.24-5.44 ppm (>NC*H*$_2$OC(=O)-, 2H). **PNAEtP** (Figure S12): δ = 1.35-2.55 ppm (methylene of main chain, 2H; methine of main chain, 1H; -NCH$_2$C*H*$_2$CH$_2$C(=O), 2H; -NCH$_2$CH$_2$C*H*$_2$C(=O), 2H), 3.38-3.62 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O), 2H; >NC*H*$_2$CH$_2$OC(=O)-, 2H), 4.07-4.26 ppm (>NCH$_2$C*H*$_2$OC(=O)-, 2H). **PNAPrP** (Figure S13): δ = 1.36-2.51 ppm (methylene of main chain, 2H; methine of main chain, 1H; >NCH$_2$C*H*$_2$CH$_2$OC(=O)-, 2H; -NCH$_2$C*H*$_2$CH$_2$C(=O), 2H; -NCH$_2$CH$_2$C*H*$_2$C(=O), 2H), 3.22-3.54 ppm (>NC*H*$_2$CH$_2$CH$_2$OC(=O)-, 2H; -NC*H*$_2$CH$_2$CH$_2$C(=O), 2H), 3.91-4.18 ppm (>NCH$_2$CH$_2$C*H*$_2$OC(=O)-, 2H). **PNABuP** (Figure S14): δ = 1.34-2.49 ppm (methylene of main chain, 2H; methine of main chain, 1H; >N CH$_2$CH$_2$C*H*$_2$CH$_2$OC(=O)-, 2H; >NCH$_2$C*H*$_2$CH$_2$CH$_2$OC(=O)-, 2H; -NCH$_2$C*H*$_2$CH$_2$C(=O), 2H; -NCH$_2$CH$_2$C*H*$_2$C(=O), 2H), 3.22-3.51 ppm (>NC*H*$_2$CH$_2$CH$_2$CH$_2$OC(=O)-, 2H; -NC*H*$_2$CH$_2$CH$_2$C(=O), 2H), 3.91-4.59 ppm (>NCH$_2$CH$_2$CH$_2$C*H*$_2$OC(=O)-, 2H). **PNAPnP** (Figure S15): δ = 1.24-2.47 ppm (methylene of main chain, 2H; methine of main chain, 1H; >NCH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$OC(=O)-, 2H; >NCH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$OC(=O)-, 2H; >NCH$_2$CH$_2$CH$_2$C*H*$_2$CH$_2$OC(=O)-, 2H; -NCH$_2$C*H*$_2$CH$_2$C(=O), 2H; -NCH$_2$CH$_2$C*H*$_2$C(=O), 2H), 3.24-3.33 ppm (>NC*H*$_2$CH$_2$CH$_2$CH$_2$CH$_2$OC(=O)-, 2H), 3.36-3.45 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O), 2H), 3.90-4.11 ppm (>NCH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$OC(=O)-, 2H). **PNAHxP** (Figure S16): δ = 1.22-2.50 ppm (methylene of main chain, 2H; methine of main chain, 1H; >NCH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$CH$_2$OC(=O)-, 2H; >NCH$_2$C*H*$_2$CH$_2$CH$_2$CH$_2$CH$_2$OC(=O)-, 2H; >NCH$_2$CH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$OC(=O)-, 2H; >NCH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$CH$_2$OC(=O)-, 2H; -NCH$_2$C*H*$_2$CH$_2$C(=O), 2H; -NCH$_2$CH$_2$C*H*$_2$C(=O), 2H), 3.21-3.32 ppm (>NC*H*$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$OC(=O)-, 2H), 3.34-3.44 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O), 2H), 3.88-4.12 ppm (>NCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$OC(=O)-, 2H).

The values of M_n, $Đ$, and T_g were shown in Table 1.

General method for synthesis of copolymers (P(NAR$_1$P$_x$-*co*-NAR$_2$P$_{100-x}$)) by radical polymerization

In a typical synthesis of P(NAR$_1$P$_x$-*co*-NAR$_2$P$_{100-x}$), NARPs (total of 6 mmol), whose feed composition is shown in Table 2 and S1, with AIBN (1/200 equiv.) were dissolved in DMF. The solutions were poured into a two-neck flask at a constant monomer concentration of 2 M, and deoxygenated by bubbling dry Ar for 30 min. Then, the reaction mixtures were placed in a preheated oil bath at 60 °C. After polymerization for 40 min, the mixtures were cooled to room temperature and poured into a large excess of diethyl ether to precipitate P(NAR$_1$P$_x$-*co*-NAR$_2$P$_{100-x}$)s. The resultant copolymers were further purified by reprecipitation method from the methanol/diethyl ether system. The solvents were removed in *vacuo* to obtain the pure copolymers as a colorless viscous liquid. The chemical structure and component of the copolymers was characterized by ^{1}H NMR spectroscopy. The values of M_n and $Đ$ were estimated from SEC analysis. The T_gs were determined by DSC measurement.

^{1}H NMR [400 MHz, chloroform-*d*, TMS] (Figure S19-S22, S24-S37): **P(NAMeP$_x$-*co*-NAPrP$_{100-x}$)** (x means composition of NAMeP unit): δ = 1.38-2.53 ppm (methylene of main chain , 2(x/100) + 2((100-x)/100)H; methine of main chain, (x/100) + ((100-x)/100)H; -NCH$_2$C*H*$_2$CH$_2$C(=O) of PNAMeP, 2(x/100)H; -NCH$_2$CH$_2$C*H*$_2$C(=O) of PNAMeP, 2(x/100)H); >NCH$_2$C*H*$_2$CH$_2$OC(=O)- of PNAPrP, 2((100-x)/100)H; -NCH$_2$C*H*$_2$CH$_2$C(=O) of PNAPrP, 2((100-x)/100)H; -NCH$_2$CH$_2$C*H*$_2$C(=O) of PNAPrP, 2((100-x)/100)H), 3.22-3.49 ppm (>NC*H*$_2$CH$_2$CH$_2$OC(=O)- of PNAPrP, 2((100-x)/100)H; -NC*H*$_2$CH$_2$CH$_2$C(=O) of PNAPrP, 2((100-x)/100)H), 3.50-3.60 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O) of PNAMeP, 2(x/100)H), 3.95-4.16 ppm (>NCH$_2$CH$_2$C*H*$_2$OC(=O)- of PNAPrP, 2((100-x)/100)H), 5.21-5.41 ppm (>NC*H*$_2$OC(=O)- of PNAMeP, 2(x/100)H). **P(NAEtP$_x$-*co*-NAHxP$_{100-x}$)** (x means composition of NAEtP unit): δ = 1.22-2.49 ppm (methylene of main chain , 2(x/100) + 2((100-x)/100)H; methine of main chain, (x/100) + ((100-x)/100)H; -NCH$_2$C*H*$_2$CH$_2$C(=O) of PNAEtP, 2(x/100)/H; -NCH$_2$CH$_2$C*H*$_2$C(=O) of PNAEtP, 2(x/100)H; >NCH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$CH$_2$OC(=O)- of PNAHxP, 2((100-x)/100)H; >NCH$_2$C*H*$_2$CH$_2$CH$_2$CH$_2$CH$_2$OC(=O)- of PNAHxP, 2((100-x)/100)H; >NCH$_2$CH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$OC(=O)- of PNAHxP, 2((100-x)/100)H; >NCH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$CH$_2$OC(=O)- of PNAHxP, 2((100-x)/100)H; -NCH$_2$C*H*$_2$CH$_2$C(=O) of PNAHxP, 2((100-x)/100)H; -NCH$_2$CH$_2$C*H*$_2$C(=O) of PNAHxP, 2((100-x)/100)H), 3.21-3.32 ppm (>NC*H*$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$OC(=O)- of PNAHxP, 2((100-x)/100)H), 3.34-3.44 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O) of PNAHxP, 2((100-x)/100)H), 3.45-3.63 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O) of PNAEtP, 2(x/100)H; >NC*H*$_2$CH$_2$OC(=O)- of PNAEtP, 2(x/100)H), 3.88-4.12 ppm (>NCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$OC(=O)- of PNAHxP, 2((100-x)/100)H), 4.09-4.25 ppm (>NCH$_2$C*H*$_2$OC(=O)- of PNAEtP,). **P(NAPrP$_x$-*co*-NABuP$_{100-x}$)** (x means composition of NAPrP unit): δ = 1.38-2.49 ppm (methylene of main chain , 2(x/100) + 2((100-x)/100)H; methine of main chain, (x/100) + ((100-x)/100)H; >NCH$_2$C*H*$_2$CH$_2$OC(=O)- of PNAPrP, 2(x/100)H; -NCH$_2$C*H*$_2$CH$_2$C(=O) of PNAPrP, 2(x/100)H; -NCH$_2$CH$_2$C*H*$_2$C(=O) of PNAPrP, 2(x/100)H), 3.22-3.54 ppm (>NC*H*$_2$CH$_2$CH$_2$OC(=O)- of PNAPrP, 2(x/100)H; -NC*H*$_2$CH$_2$CH$_2$C(=O) of PNAPrP, 2(x/100)H; >NC*H*$_2$CH$_2$CH$_2$CH$_2$OC(=O)- of PNABuP, 2((100-x)/100)H; -NC*H*$_2$CH$_2$CH$_2$C(=O) of PNABuP, 2((100-x)/100)H), 3.94-4.19 ppm (>NCH$_2$CH$_2$C*H*$_2$OC(=O)- of PNAPrP, 2(x/100)H); >NCH$_2$CH$_2$CH$_2$C*H*$_2$OC(=O)- of PNABuP, 2((100-x)/100)H). **P(NABuP$_x$-*co*-NAPnP$_{100-x}$)** (x means composition of NABuP unit): δ = 1.27-2.46 ppm (methylene of main chain , 2(x/100) + 2((100-x)/100)H; methine of main chain, (x/100) + ((100-x)/100)H; >N CH$_2$CH$_2$C*H*$_2$CH$_2$OC(=O)- of PNABuP, 2(x/100)H; >NCH$_2$C*H*$_2$CH$_2$CH$_2$OC(=O)- of PNABuP, 2(x/100)H; -NCH$_2$C*H*$_2$CH$_2$C(=O) of PNABuP, 2(x/100)H; -NCH$_2$CH$_2$C*H*$_2$C(=O) of PNABuP, 2(x/100)H; >NCH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$OC(=O)- of PNAPnP, 2((100-x)/100)H; >NCH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$OC(=O)- of PNAPnP, 2((100-x)/100)H; >NCH$_2$CH$_2$CH$_2$C*H*$_2$CH$_2$OC(=O)- of PNAPnP, 2((100-x)/100)H; -NCH$_2$C*H*$_2$CH$_2$C(=O) of PNAPnP, 2((100-x)/100)H; -NCH$_2$CH$_2$C*H*$_2$C(=O) of PNAPnP, 2((100-x)/100)H), 3.22-3.51 ppm (>NC*H*$_2$CH$_2$CH$_2$CH$_2$OC(=O)- of PNABuP, 2(x/100)H; -NC*H*$_2$CH$_2$CH$_2$C(=O) of PNABuP, 2(x/100)H; >NC*H*$_2$CH$_2$CH$_2$CH$_2$CH$_2$OC(=O)- of PNAPnP, 2((100-x)/100)H), 3.36-3.45 ppm (-NC*H*$_2$CH$_2$CH$_2$C(=O) of PNAPnP, 2((100-x)/100)H), 3.91-4.59 ppm (>NCH$_2$CH$_2$CH$_2$C*H*$_2$OC(=O)- of PNABuP, 2(x/100)H; (>NCH$_2$CH$_2$CH$_2$CH$_2$C*H*$_2$OC(=O)- of PNAPnP, 2((100-x)/100)H).

The values of M_n, $Đ$, and T_g were shown in Table XX.

Calculation of log P value

Magenau and coworkers have demonstrated that log P/Connolly molecular surface area (SA) values can provide the log P values for predicting and assessing hydrophobicity of polymers.[S2] Therefore, the log P/SA values of PNARPs was computed for predicting polymer hydrophobicity/hydrophobicity balance according to previous reports. The log P values and Connolly molecular surface area (SA) (probe radius = 1.4 Å) of PNARPs decamers were determined with Chem3D Pro (ver. 19.1) (CambridgeSoft Corp., MA, USA) after MM2 minimization of the models. PNARPs showed the saturation of log P/SA values around decamers. Therefore, log P values of PNARPs was represented as that of the decamers.

References

S1 S. Nishimura, T. Ueda, D. Murakami and M. Tanaka, *Org. Mater.*, 2021, **3**, 214-220.

S2 A. J. D. Magenau, J. A. Richards, M. A. Pasquinelli, D. A. Savin and R. T. Mathers, *Macromolecules*, 2015, **48**, 7230-7236.

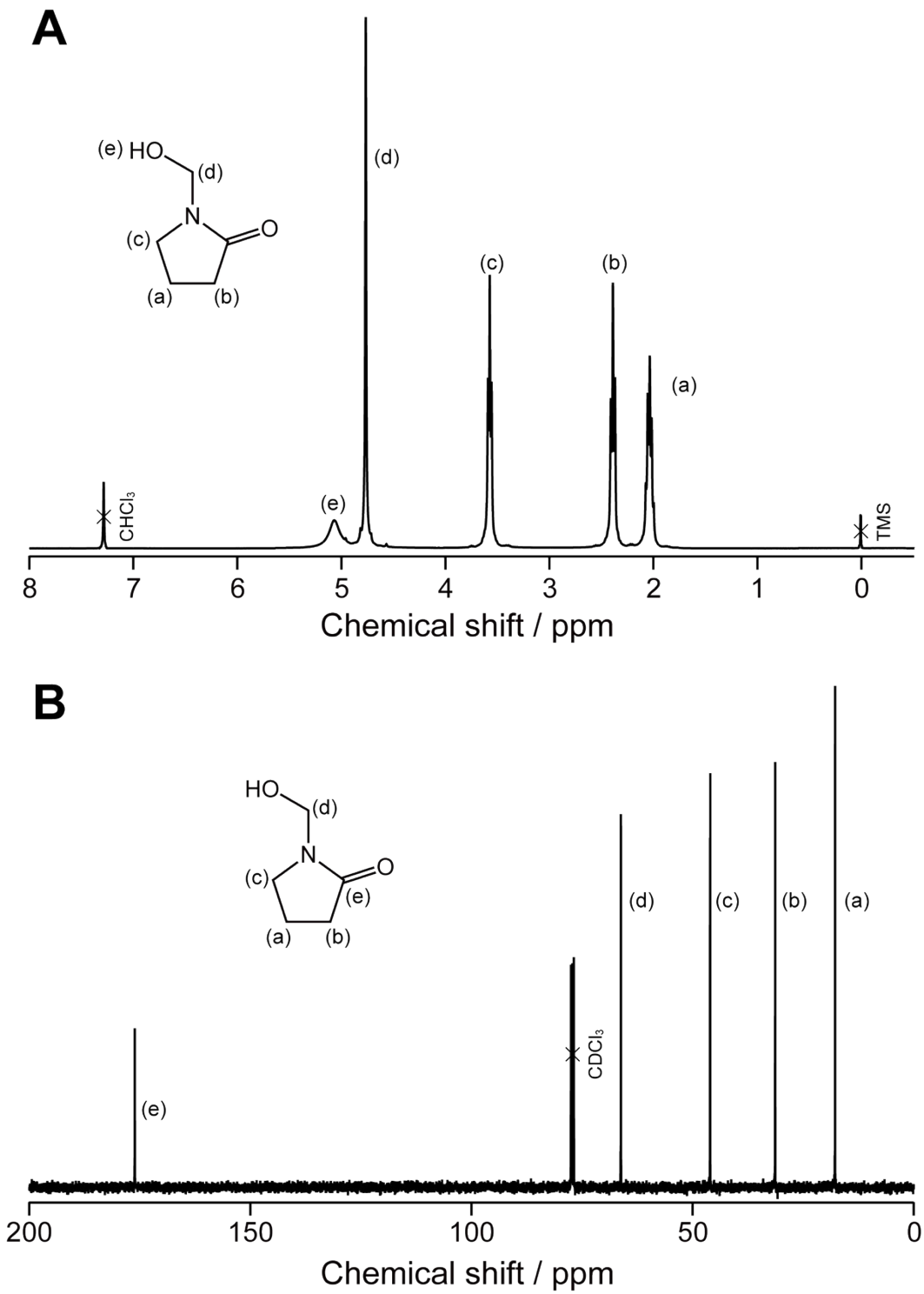

Figure S1. (A) ^{1}H and (B) ^{13}C NMR spectra of NHMeP in chloroform-*d* at 25 °C.

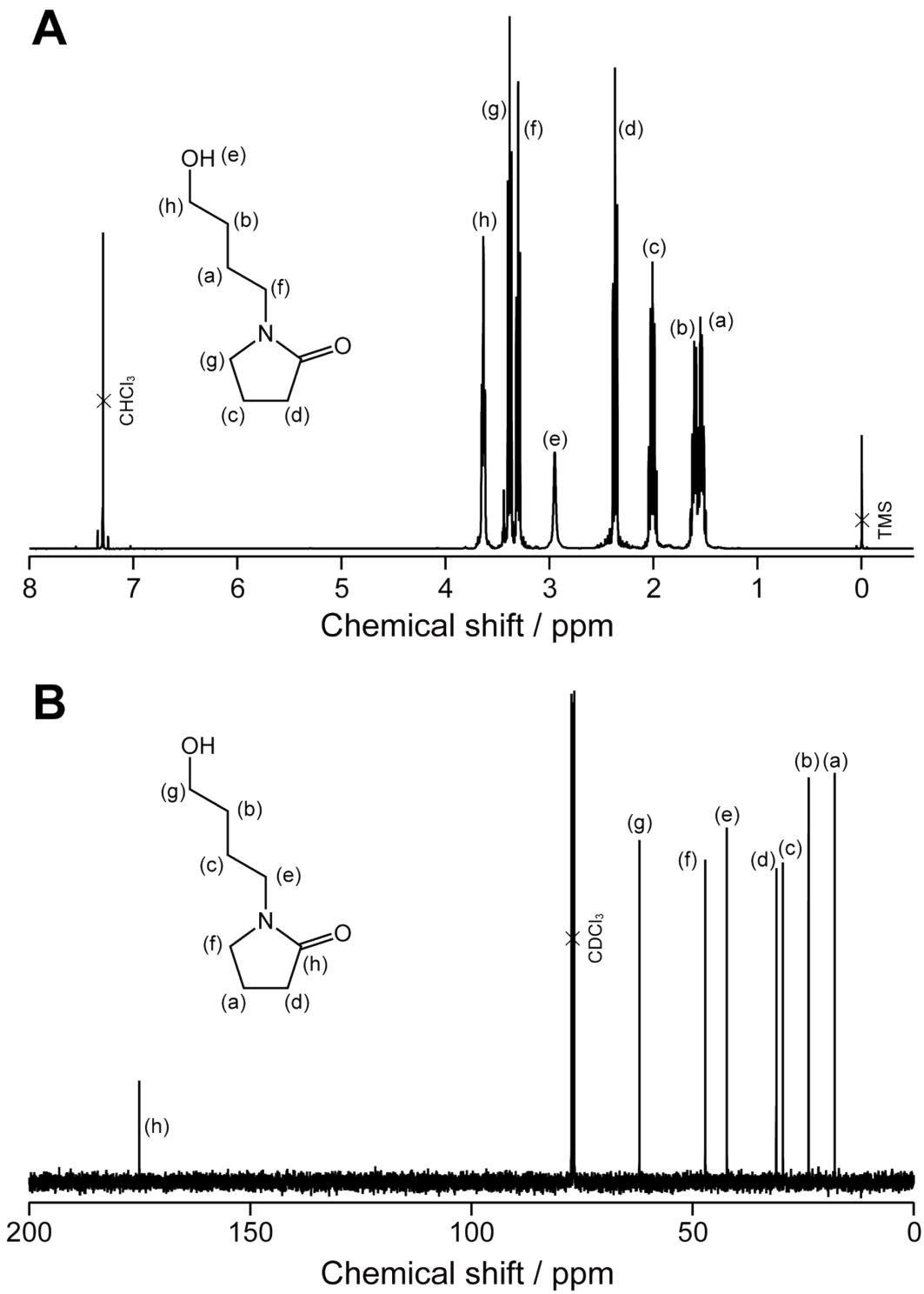

Figure S2. (A) ^{1}H and (B) ^{13}C NMR spectra of NHBuP in chloroform-*d* at 25 °C.

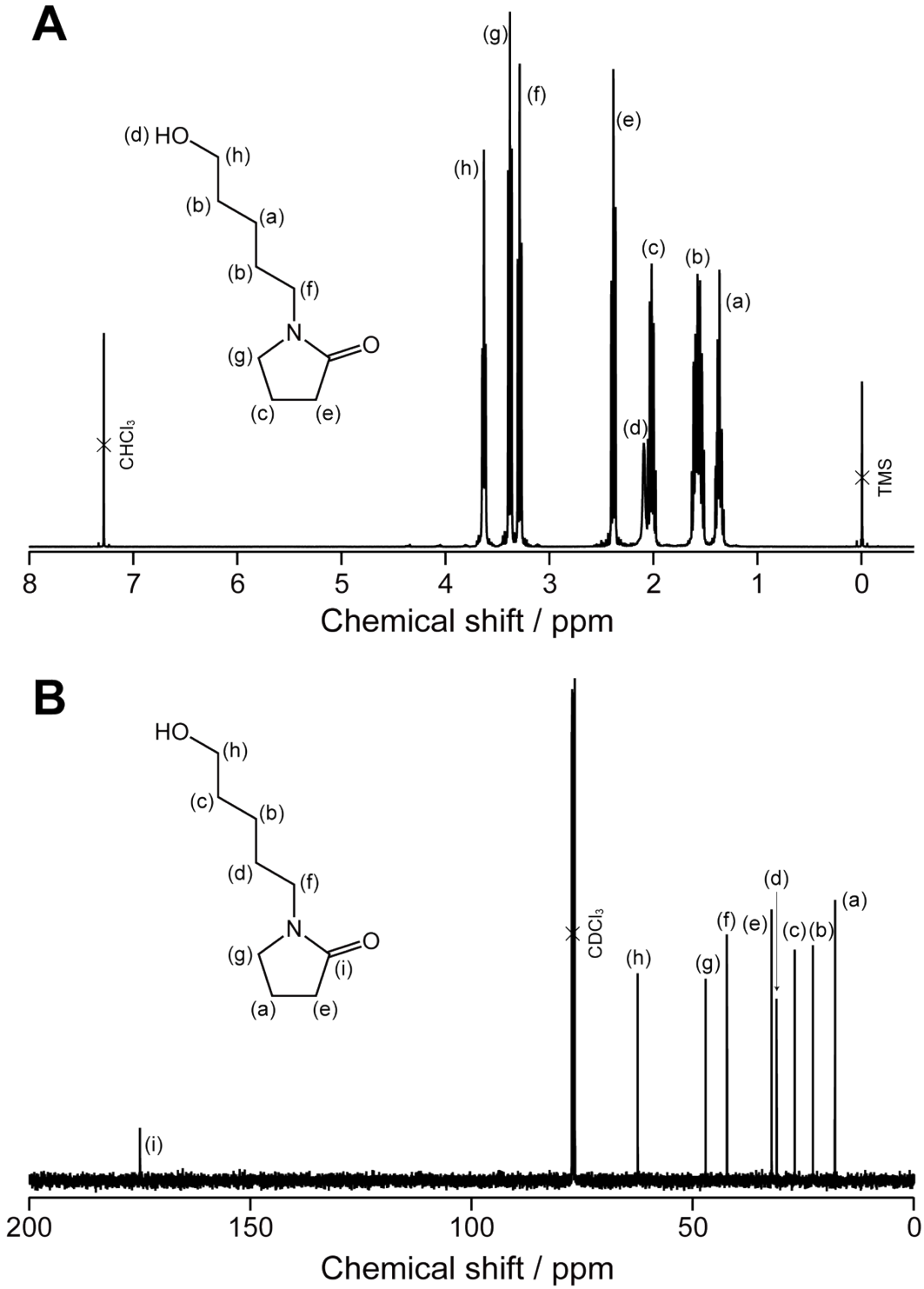

Figure S3. (A) ^{1}H and (B) ^{13}C NMR spectra of NHPnP in chloroform-*d* at 25 °C.

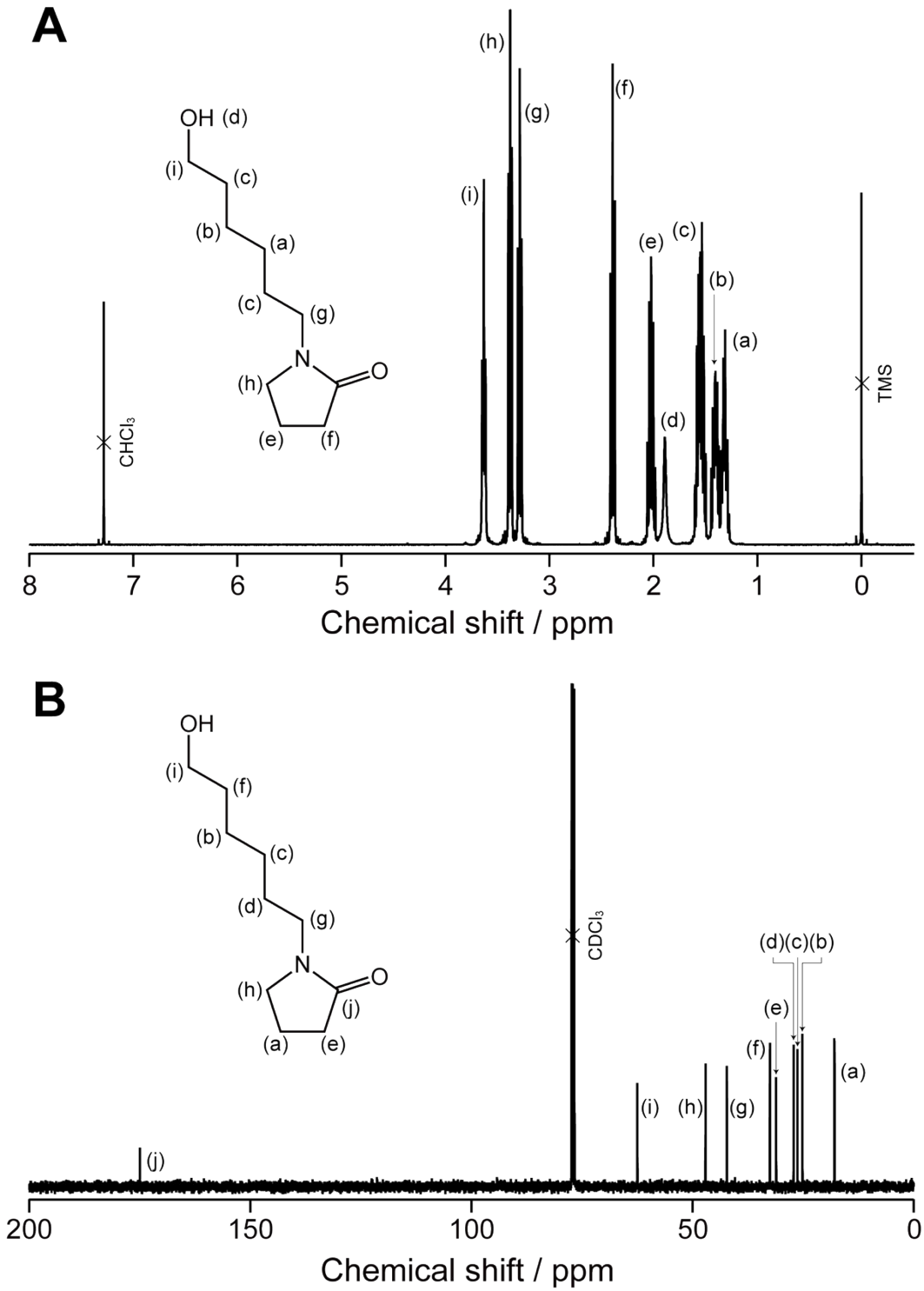

Figure S4. (A) ^{1}H and (B) ^{13}C NMR spectra of NHHxP in chloroform-*d* at 25 °C.

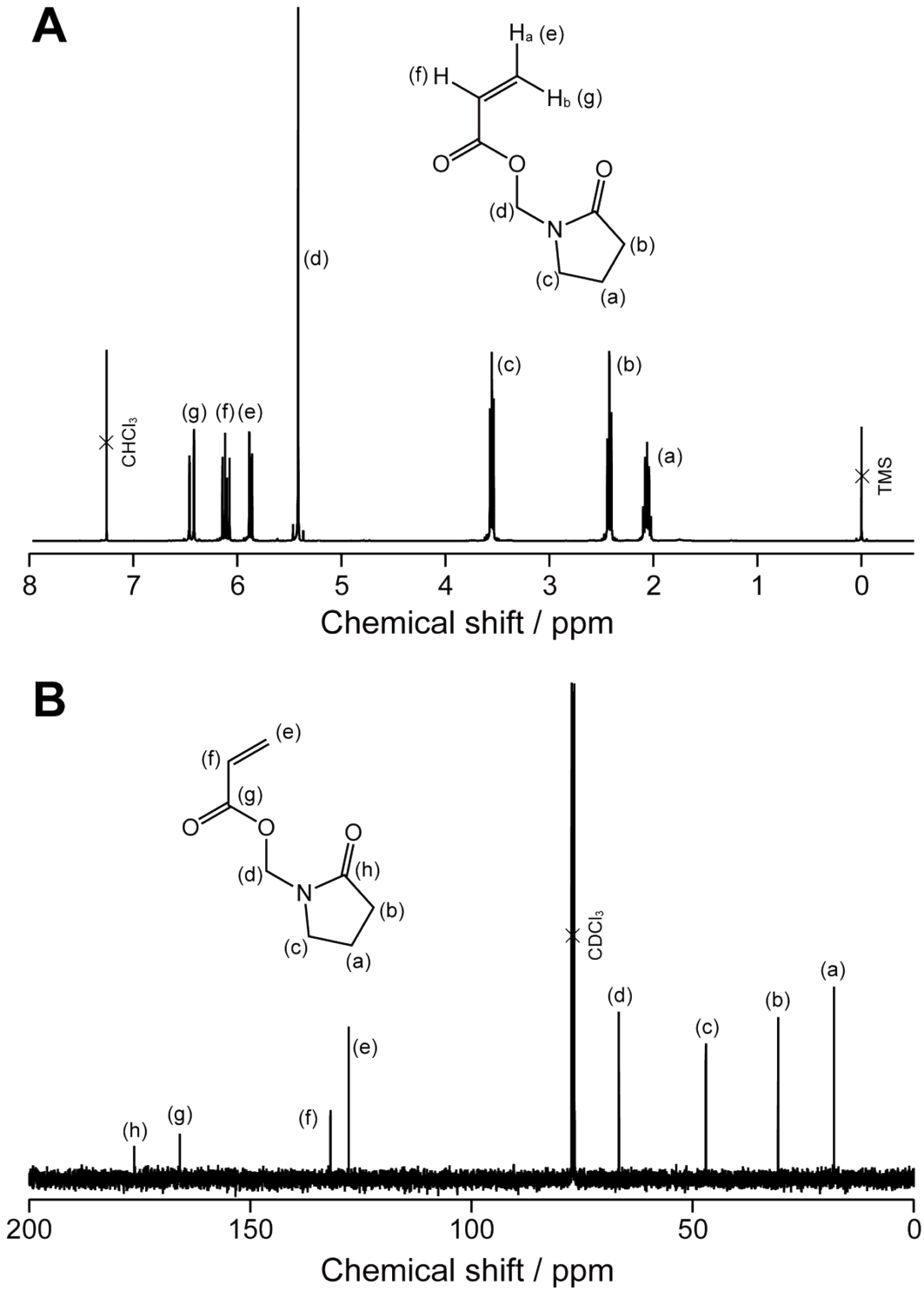

Figure S5. (A) ^{1}H and (B) ^{13}C NMR spectra of NAMeP in chloroform-*d* at 25 °C.

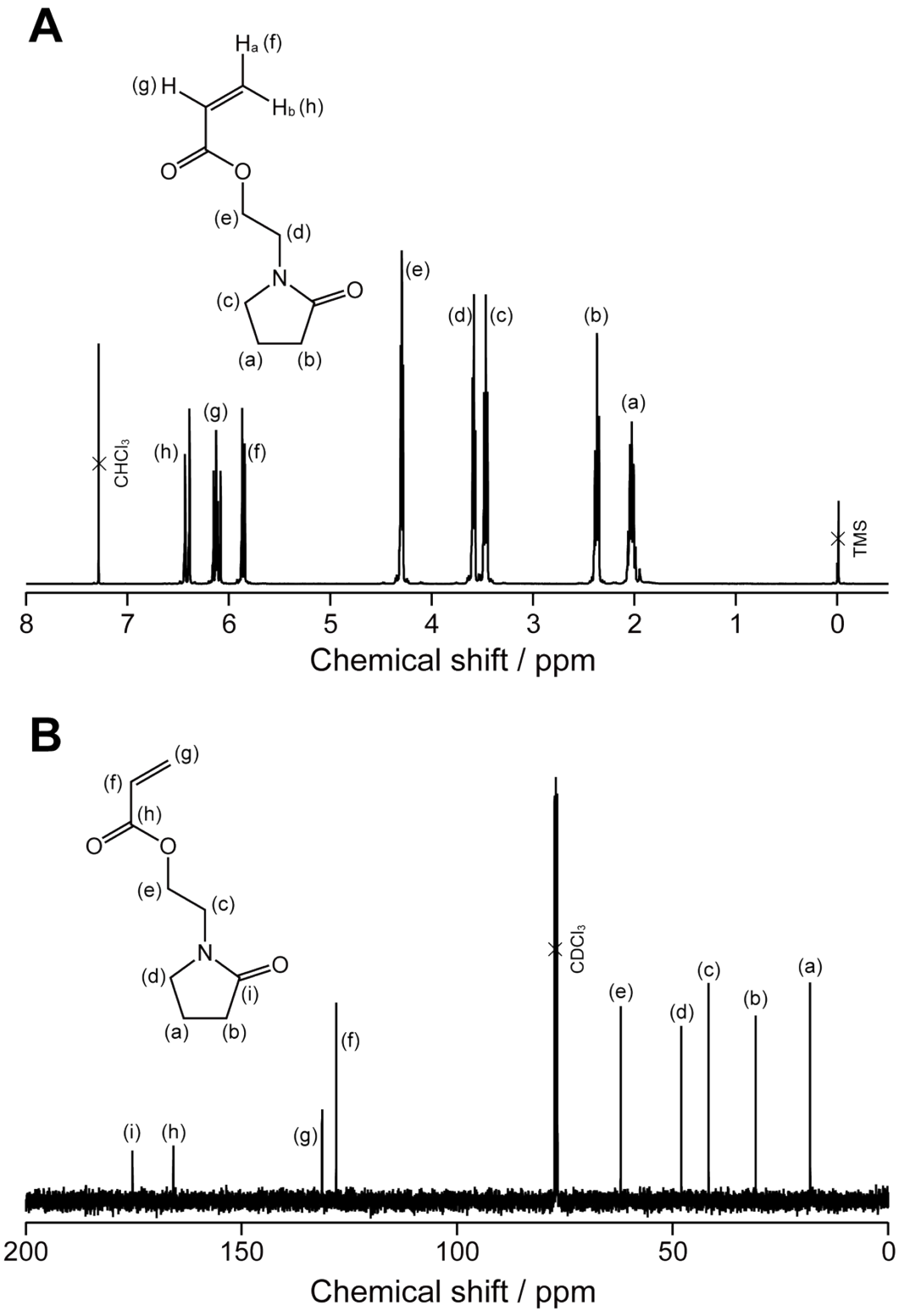

Figure S6. (A) ^{1}H and (B) ^{13}C NMR spectra of NAEtP in chloroform-*d* at 25 °C.

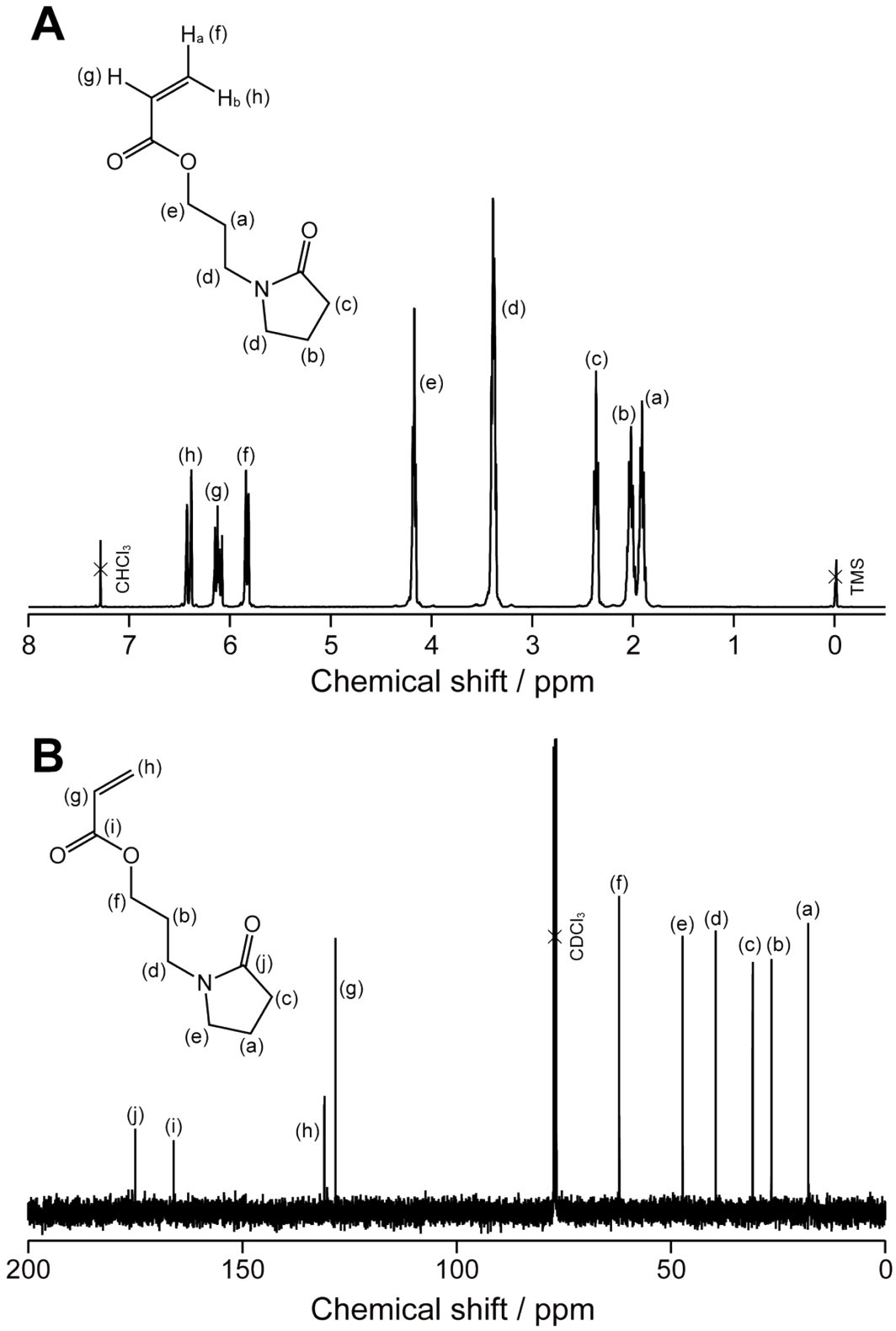

Figure S7. (A) ^{1}H and (B) ^{13}C NMR spectra of NAPrP in chloroform-*d* at 25 °C.

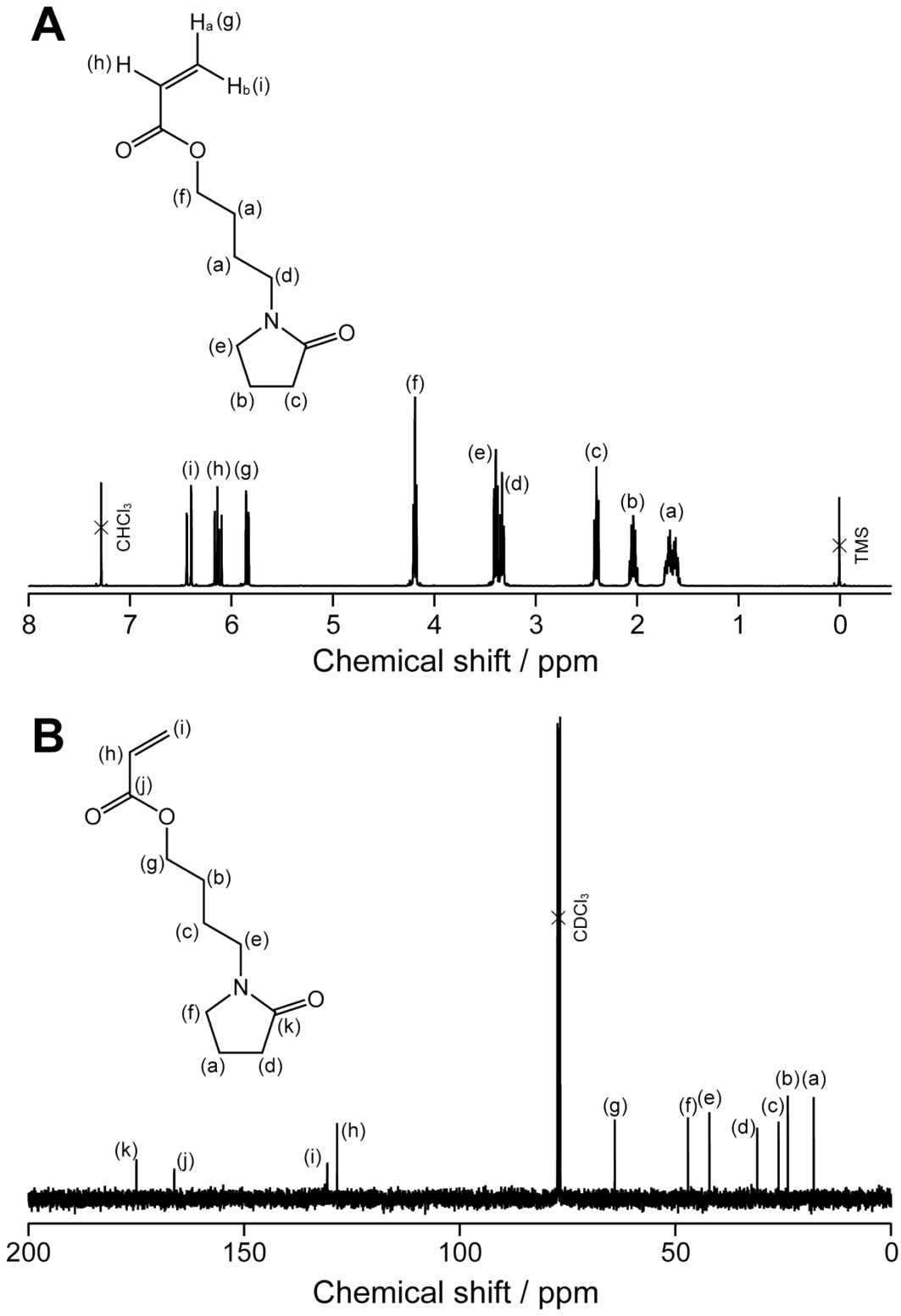

Figure S8. (A) ^{1}H and (B) ^{13}C NMR spectra of NABuP in chloroform-*d* at 25 °C.

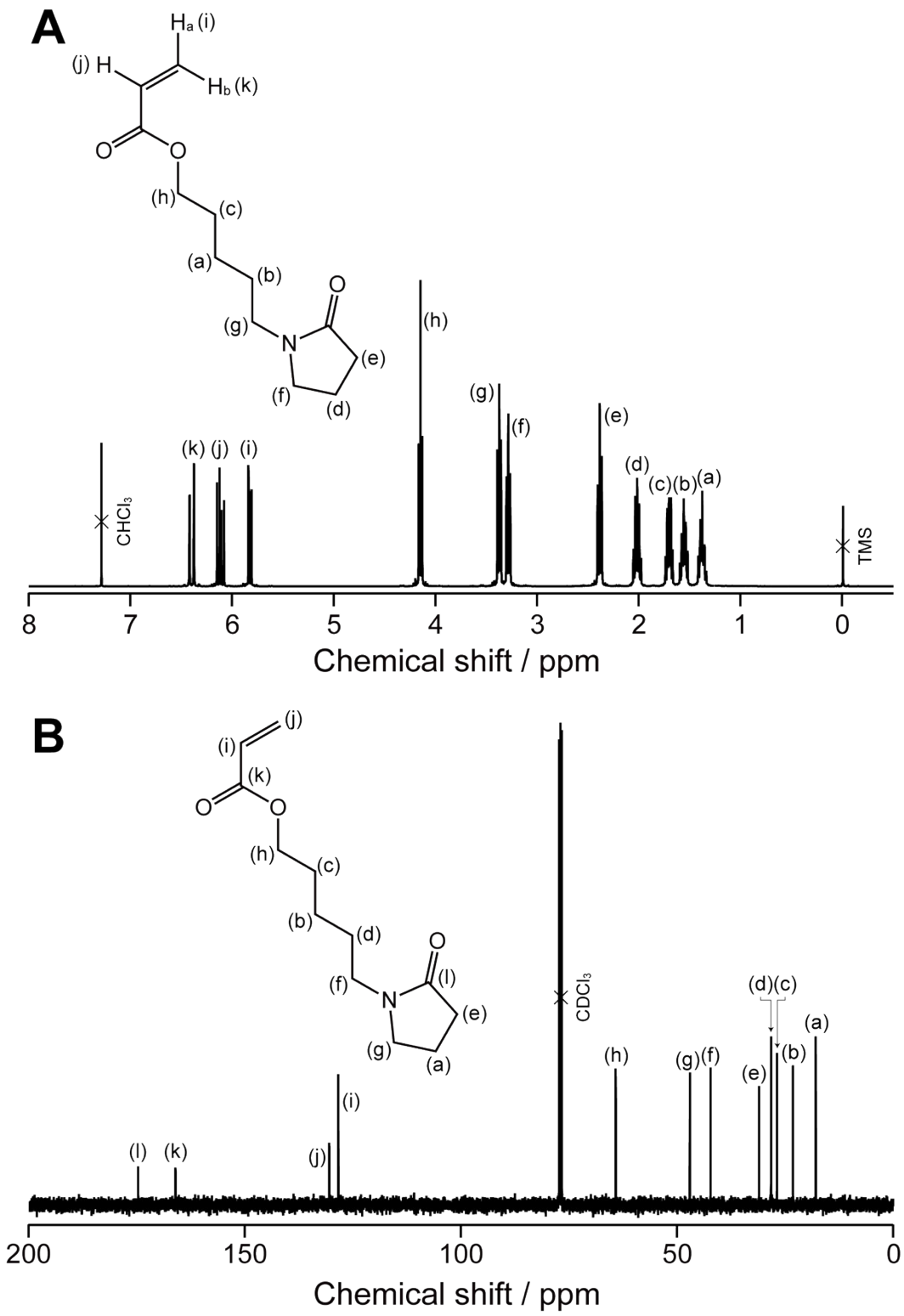

Figure S9. (A) ^{1}H and (B) ^{13}C NMR spectra of NAPnP in chloroform-*d* at 25 °C.

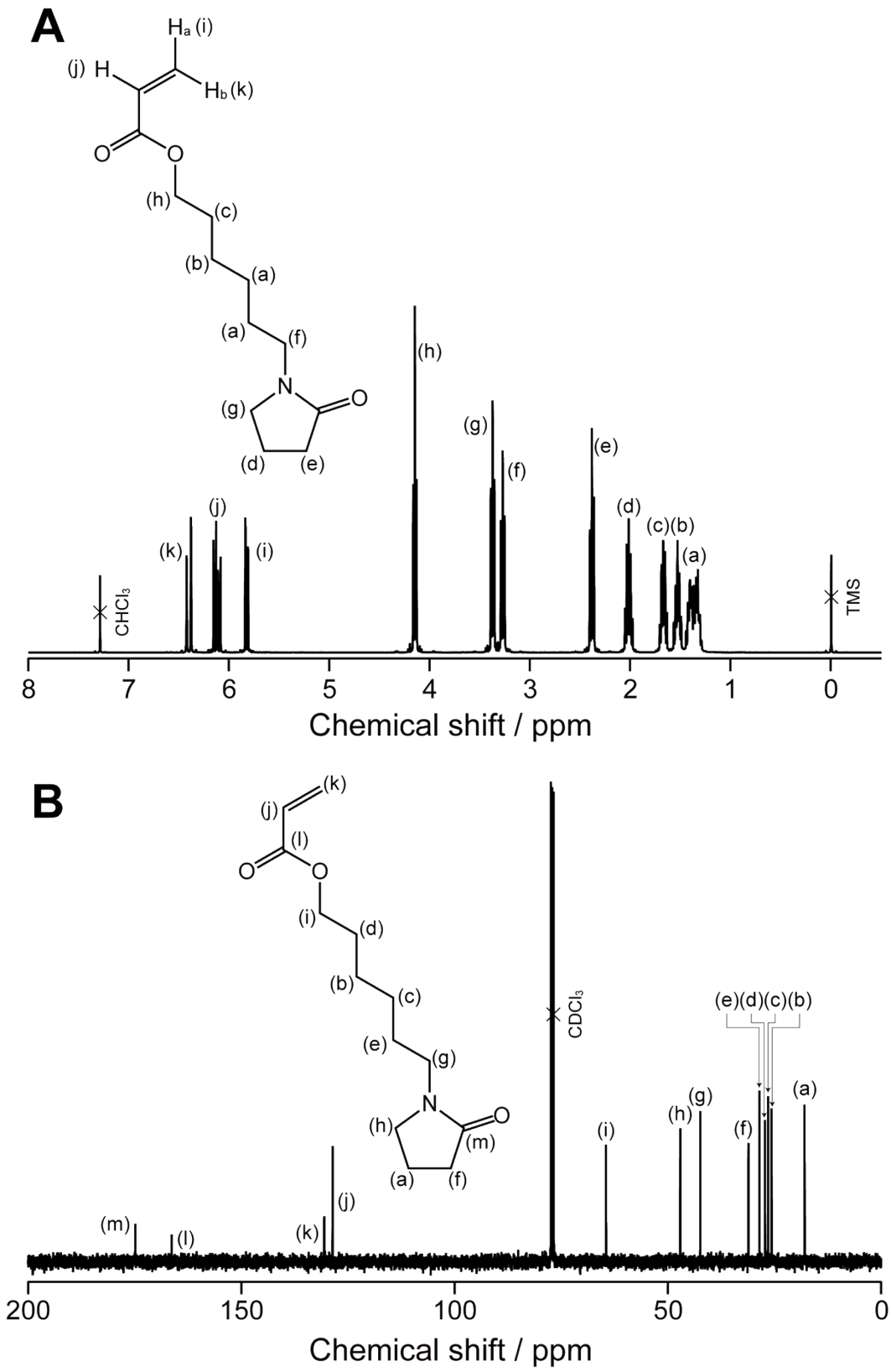

Figure S10. (A) ^{1}H and (B) ^{13}C NMR spectra of NAHxP in chloroform-*d* at 25 °C.

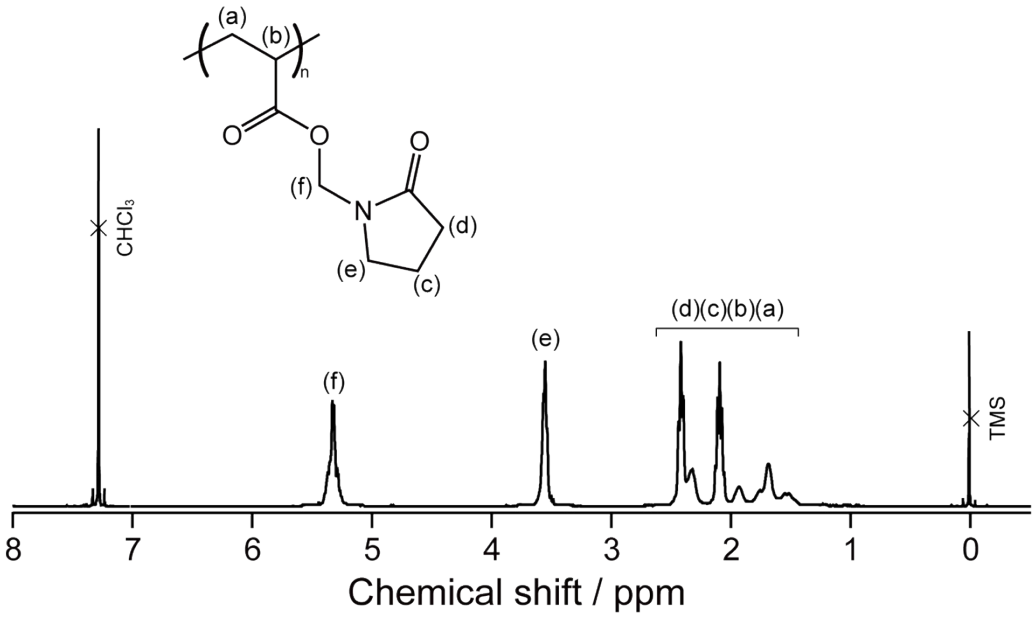

Figure S11. (A) ^{1}H NMR spectrum of PNAMeP in chloroform-*d* at 25 °C.

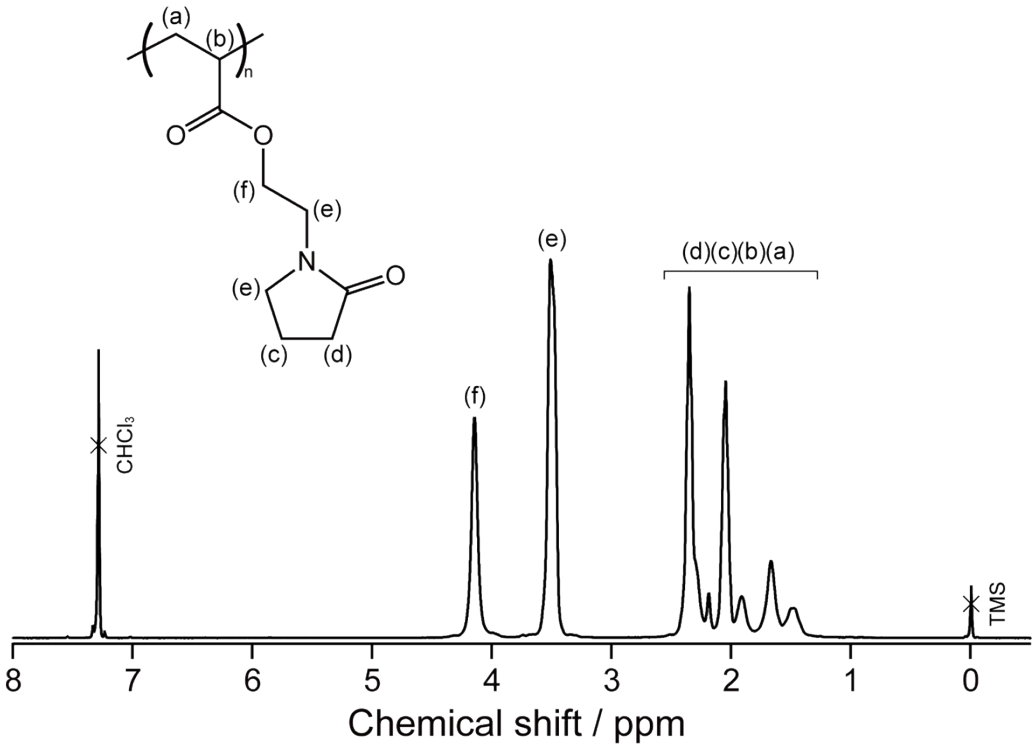

Figure S12. (A) ^{1}H NMR spectrum of PNAEtP in chloroform-*d* at 25 °C.

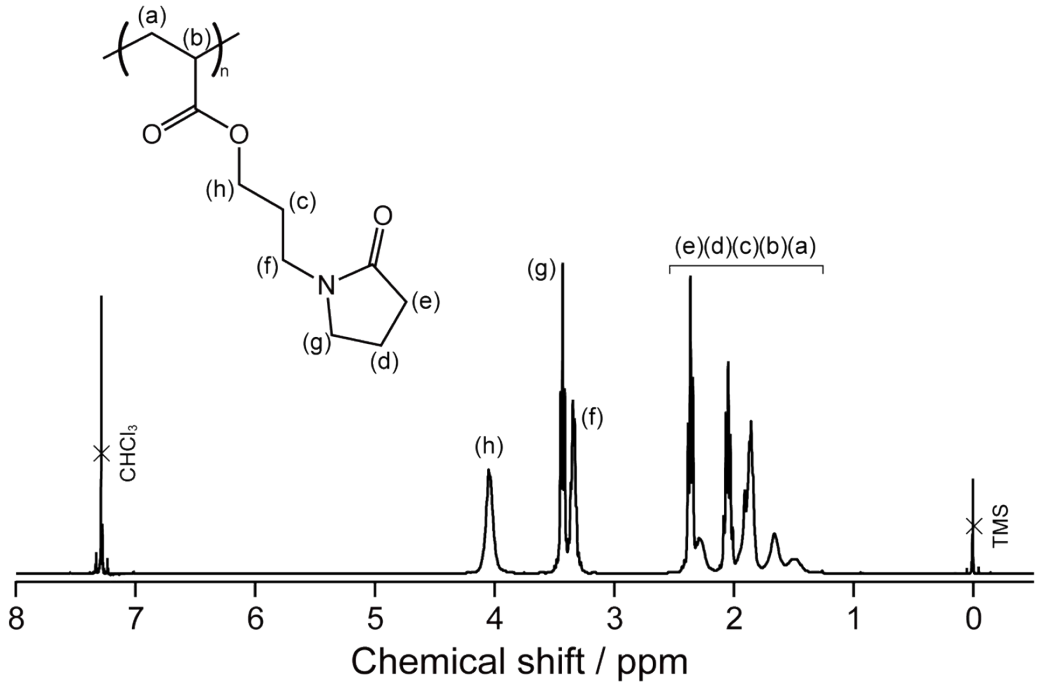

Figure S13. (A) ^{1}H NMR spectrum of PNAPrP in chloroform-*d* at 25 °C.

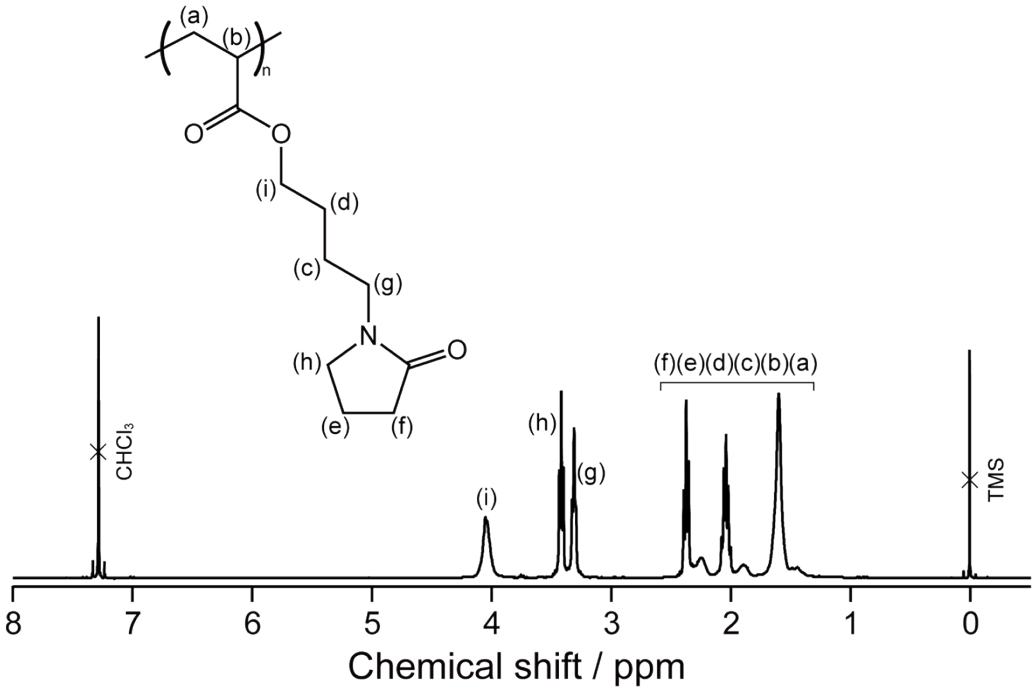

Figure S14. (A) ^{1}H NMR spectrum of PNABuP in chloroform-*d* at 25 °C.

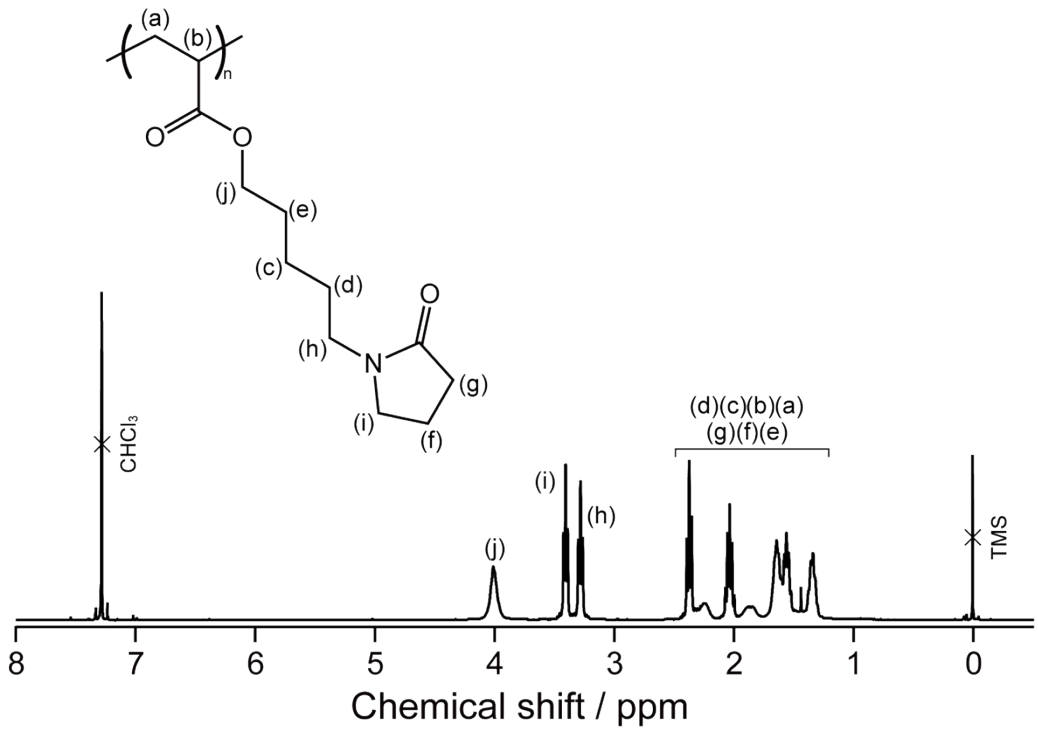

Figure S15. (A) ^{1}H NMR spectrum of PNAPnP in chloroform-*d* at 25 °C.

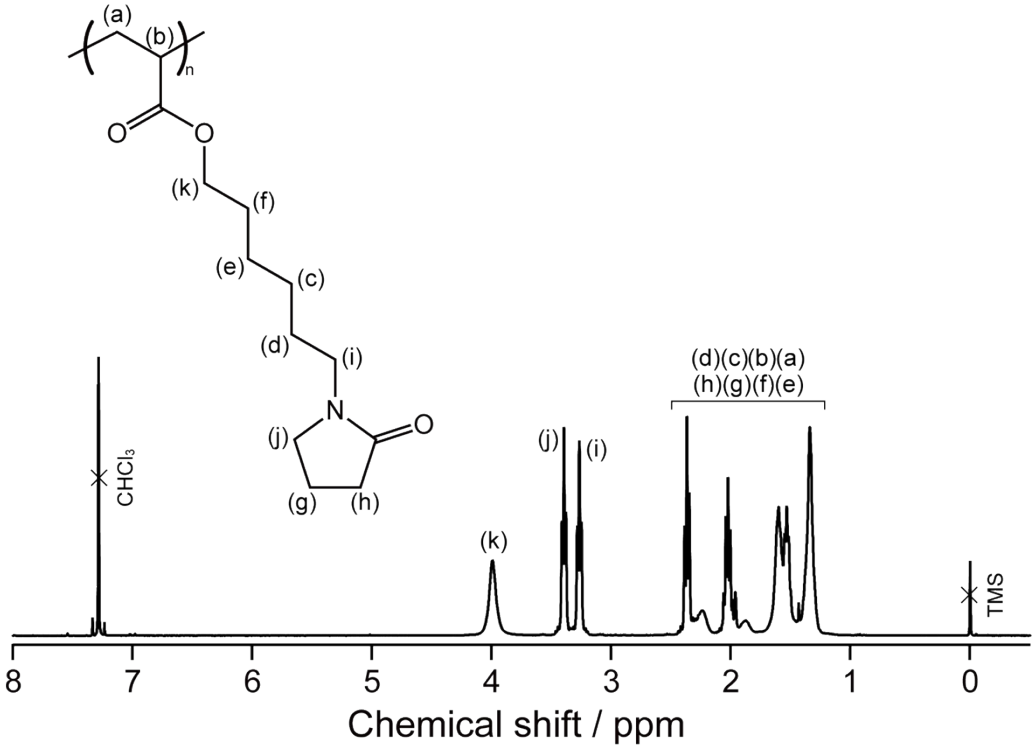

Figure S16. (A) ^{1}H NMR spectrum of PNAHxP in chloroform-*d* at 25 °C.

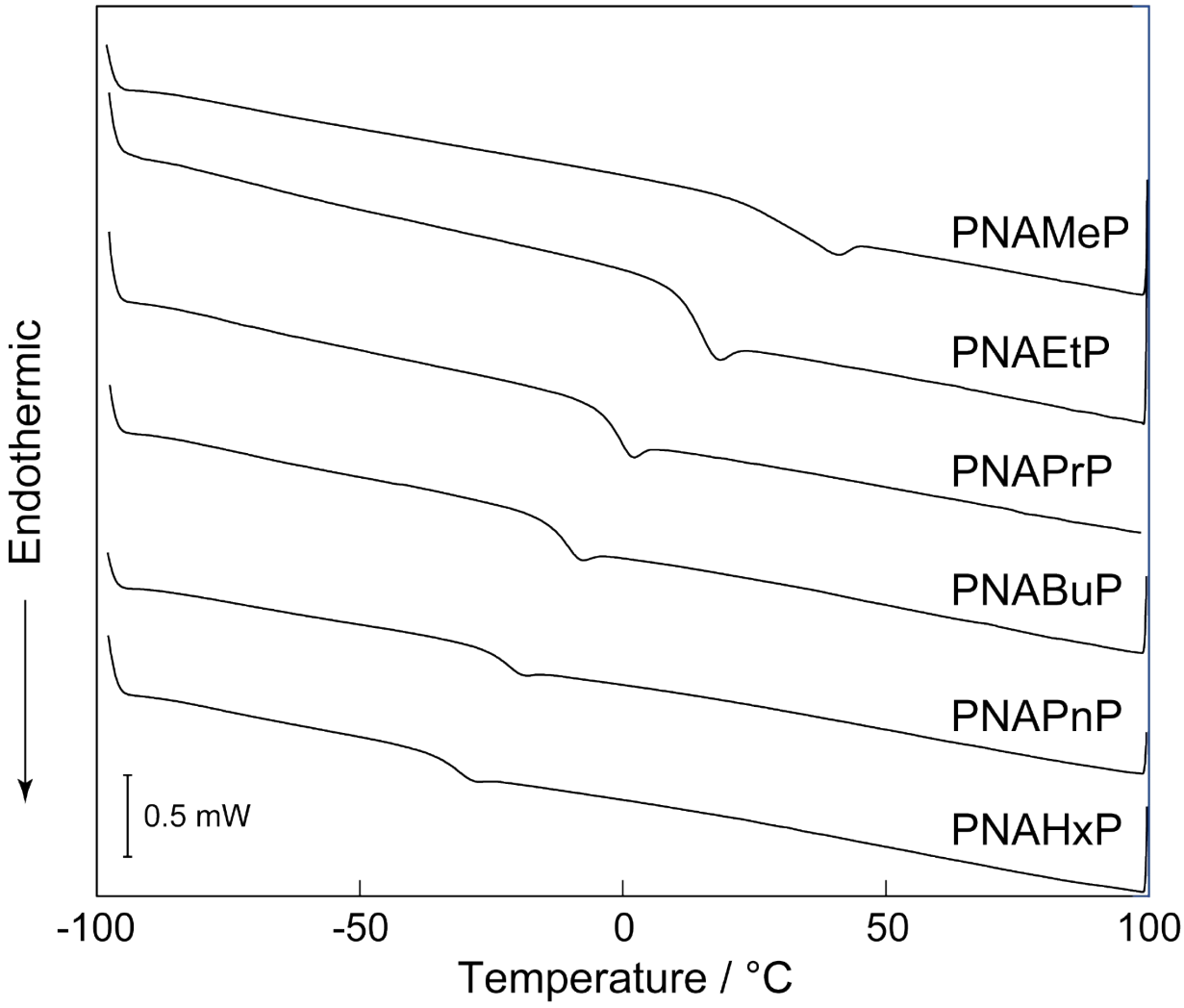

Figure S17. DSC thermograms of PNARPs under dry condition at a heating rate of 5 °C min^{-1}.

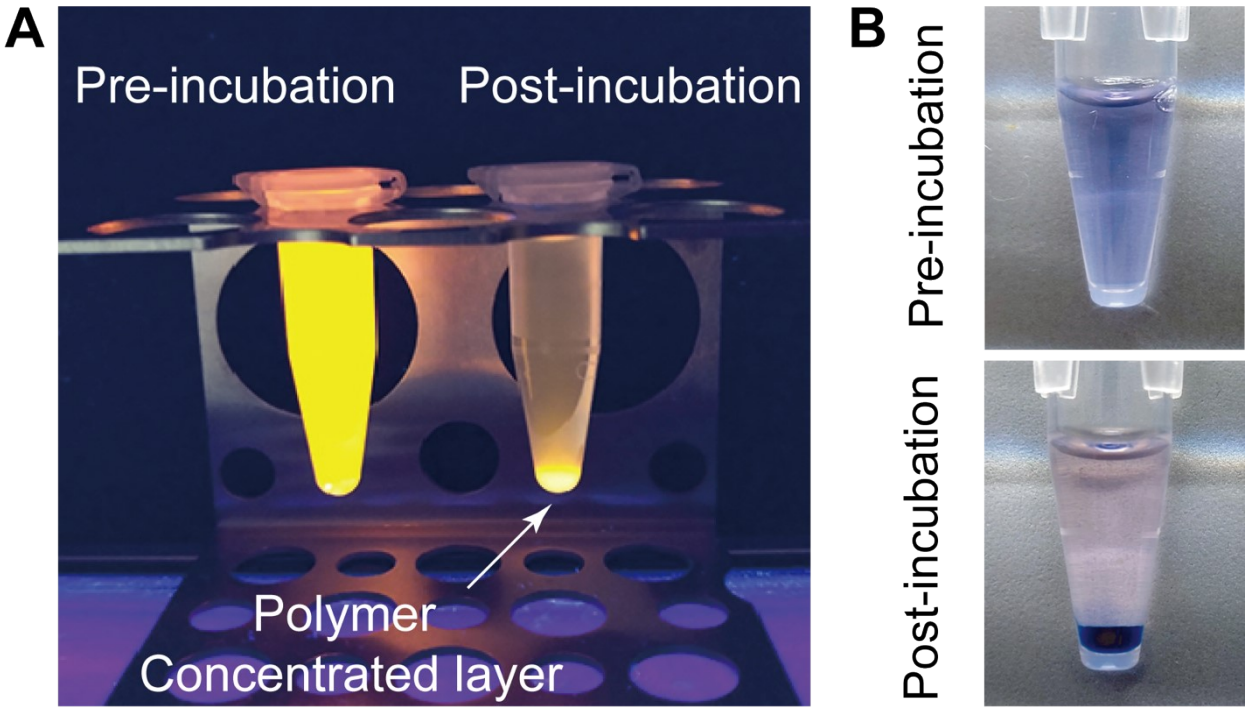

Figure S18. Photographs of (A) rhodamine B and (B) proteins with PNABuP aqueous solution (1 wt%) below and above LCST. The solutions with rhodamine B were excited by UV light (365 nm). The proteins were used a protein molecular weight marker (broad) purchased from Takara Bio Inc. (Japan).

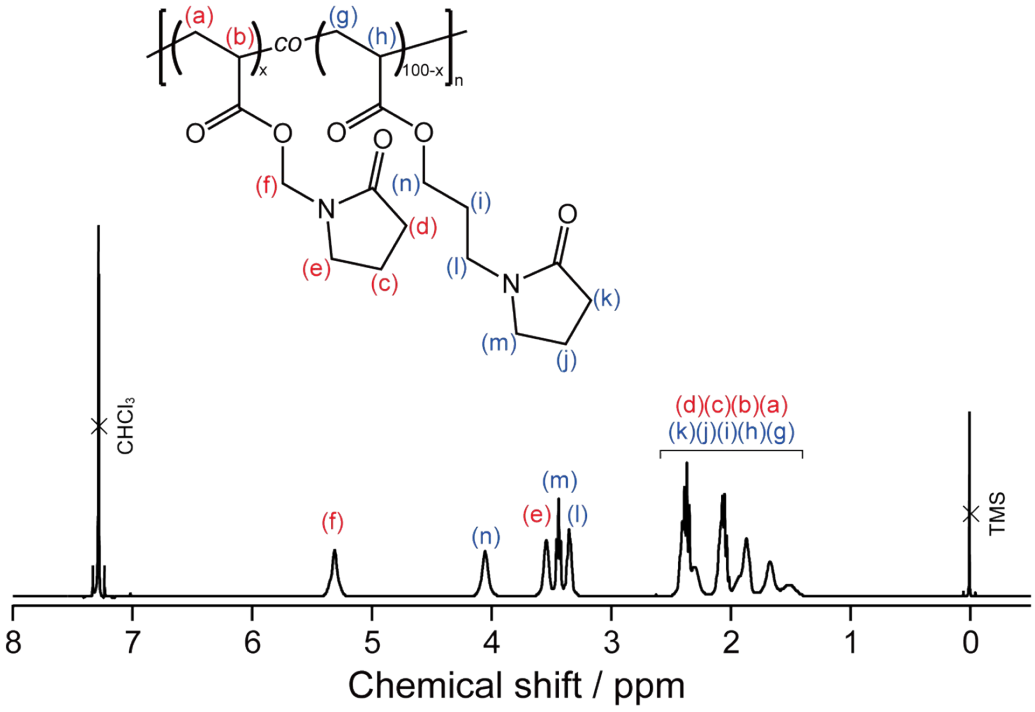

Figure S19. (A) ^{1}H NMR spectrum of PNAMeP$_{50}$-*co*-PNAPrP$_{50}$ in chloroform-*d* at 25 °C.

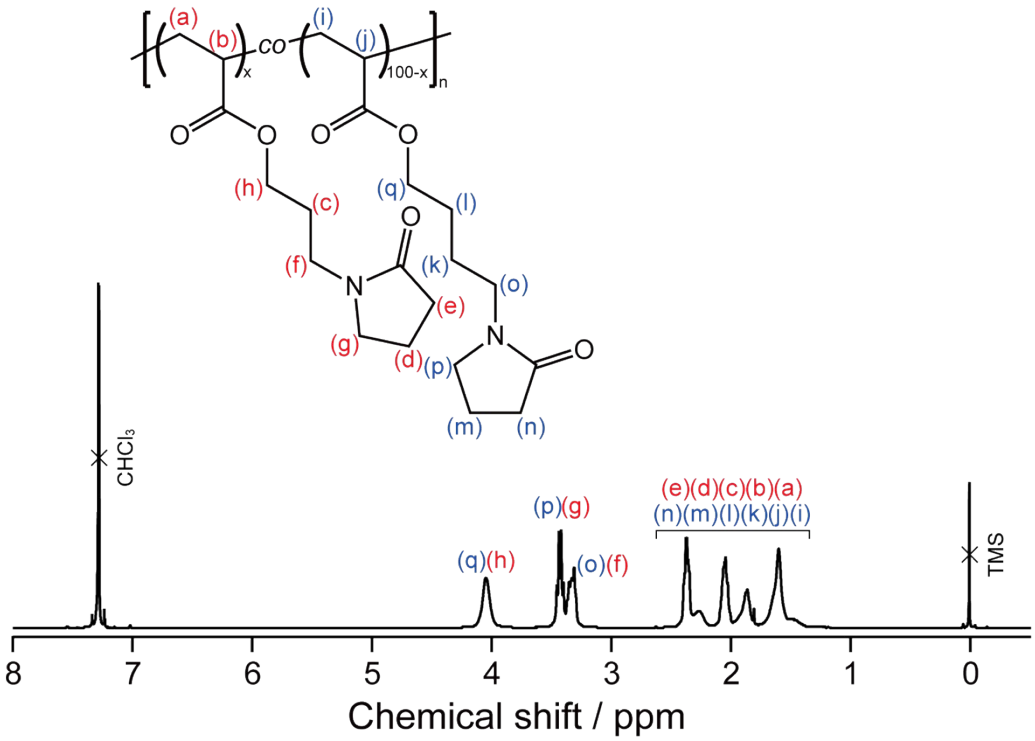

Figure S20. (A) ^{1}H NMR spectrum of PNAPrP$_{50}$-*co*-PNABuP$_{50}$ in chloroform-*d* at 25 °C.

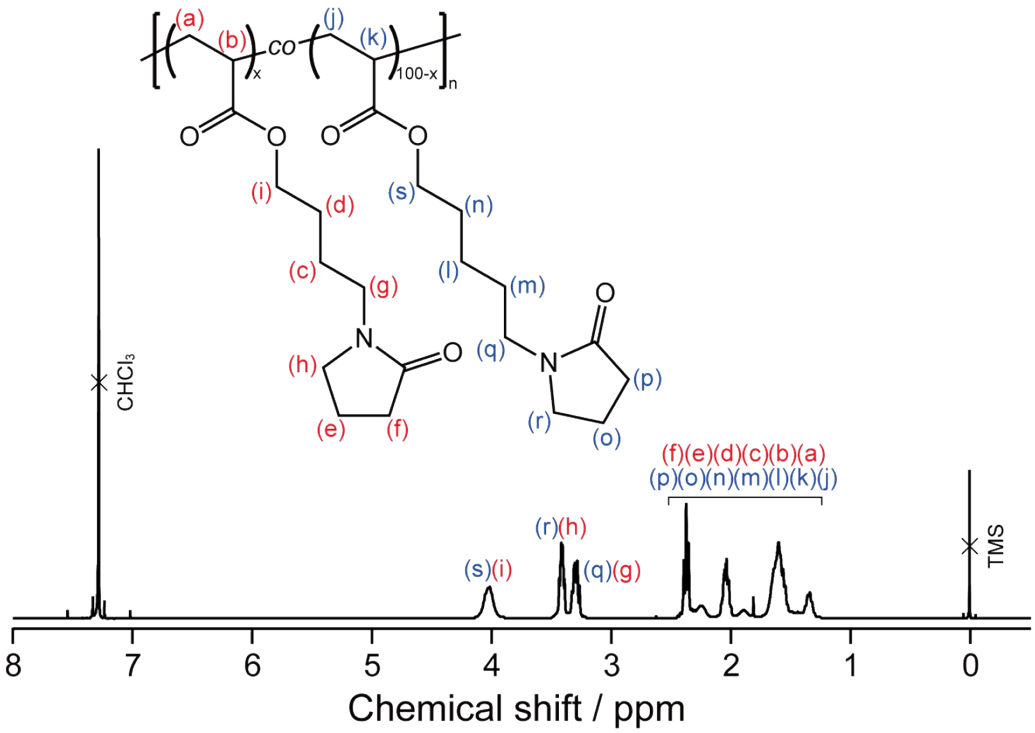

Figure S21. (A) ^{1}H NMR spectrum of PNABuP$_{50}$-*co*-PNAPnP$_{50}$ in chloroform-*d* at 25 °C.

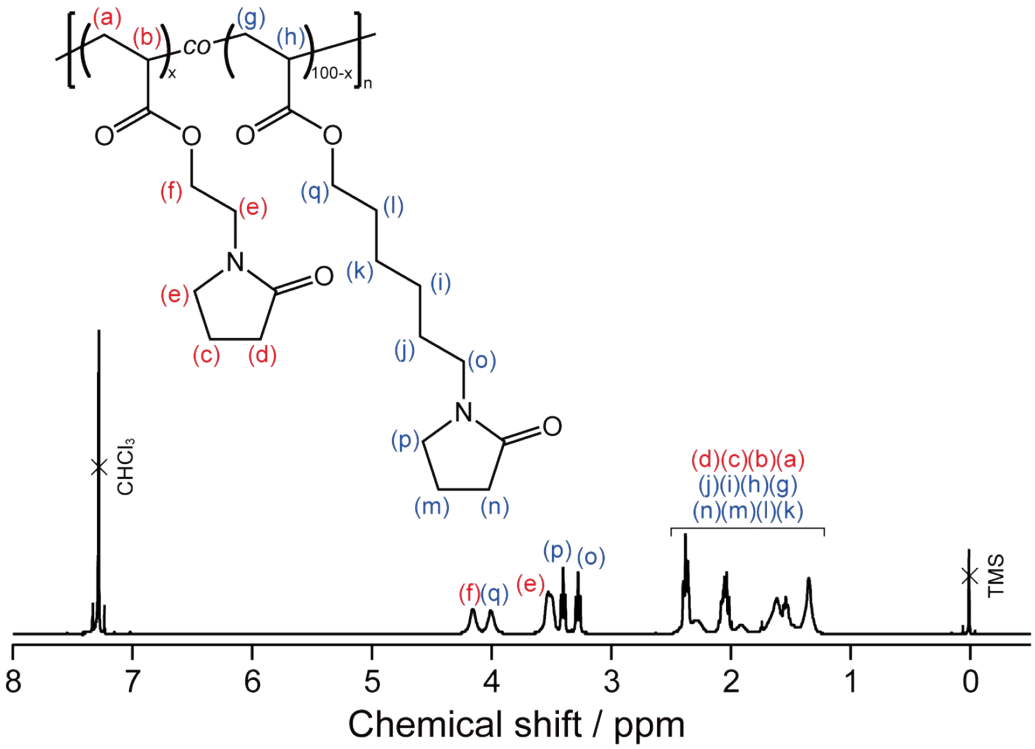

Figure S22. (A) ^{1}H NMR spectrum of PNAEtP_{50}-*co*-PNAHxP_{50} in chloroform-*d* at 25 °C.

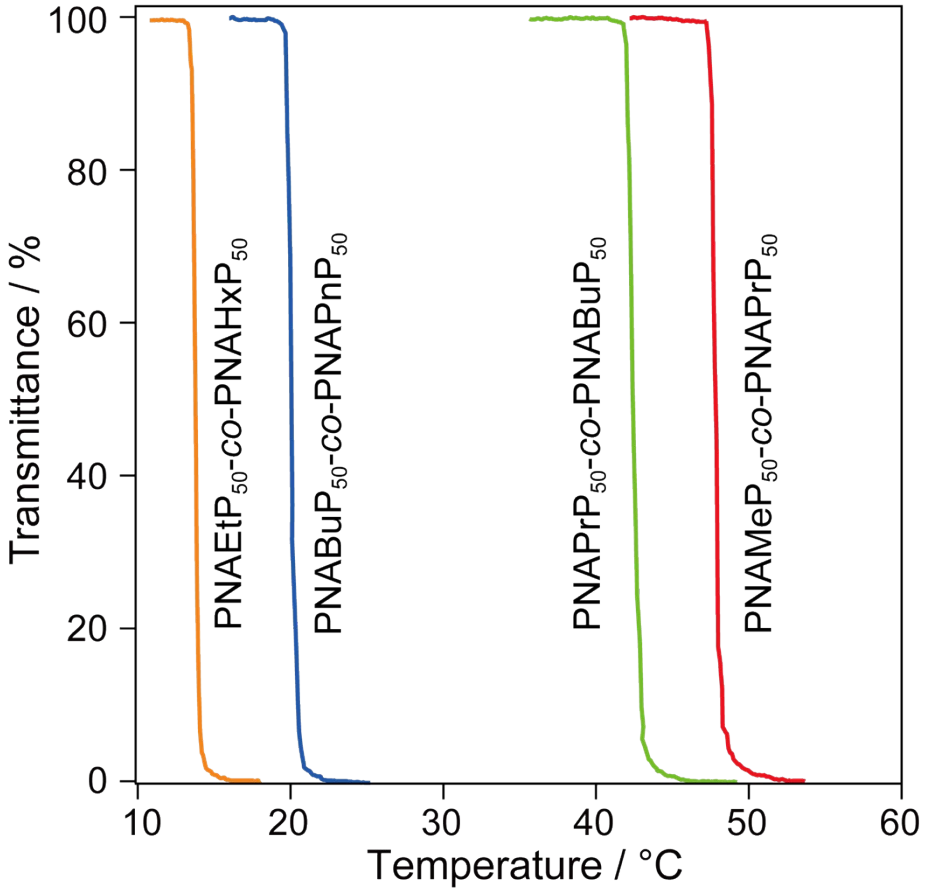

Figure S23. Thermo-responsive behavior of $PNAR_1P_{50}$-*co*-$PNAR_2P_{50}$ in water at 1.0 wt% of polymer concentration. Hating rate: 1 °C min^{-1}.

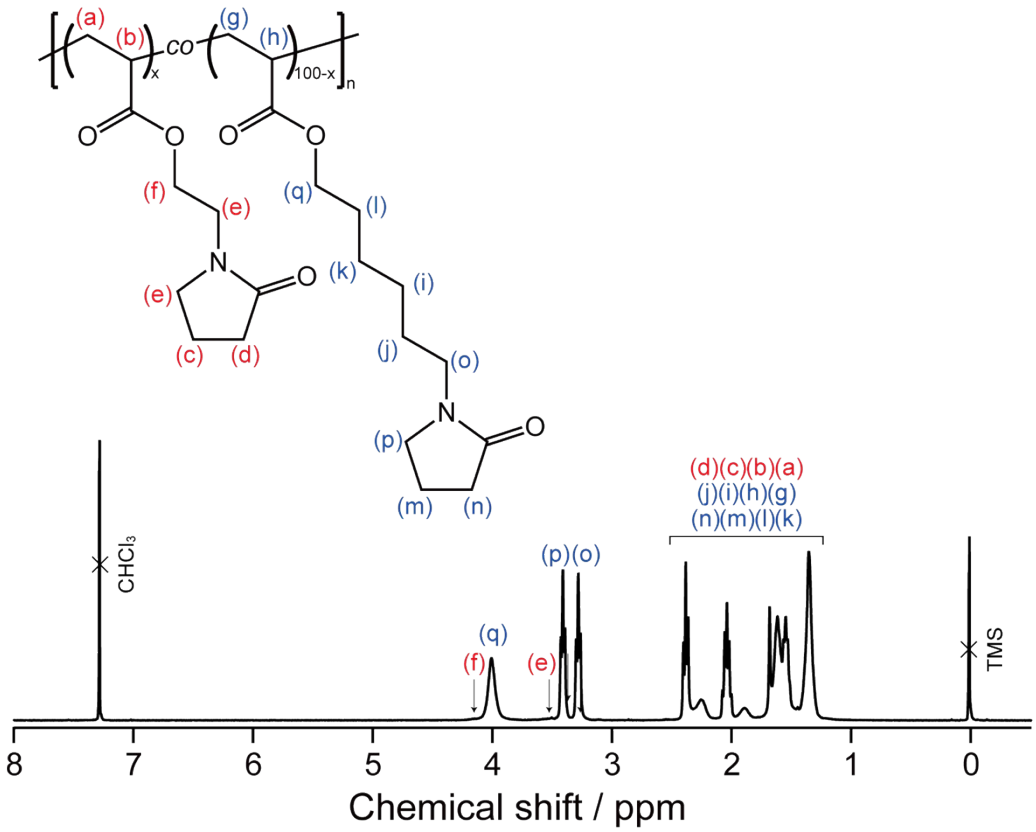

Figure S24. ^{1}H NMR spectrum of PNAEtP$_{1}$-*co*-PNAHxP$_{99}$ in chloroform-*d* at 25 °C.

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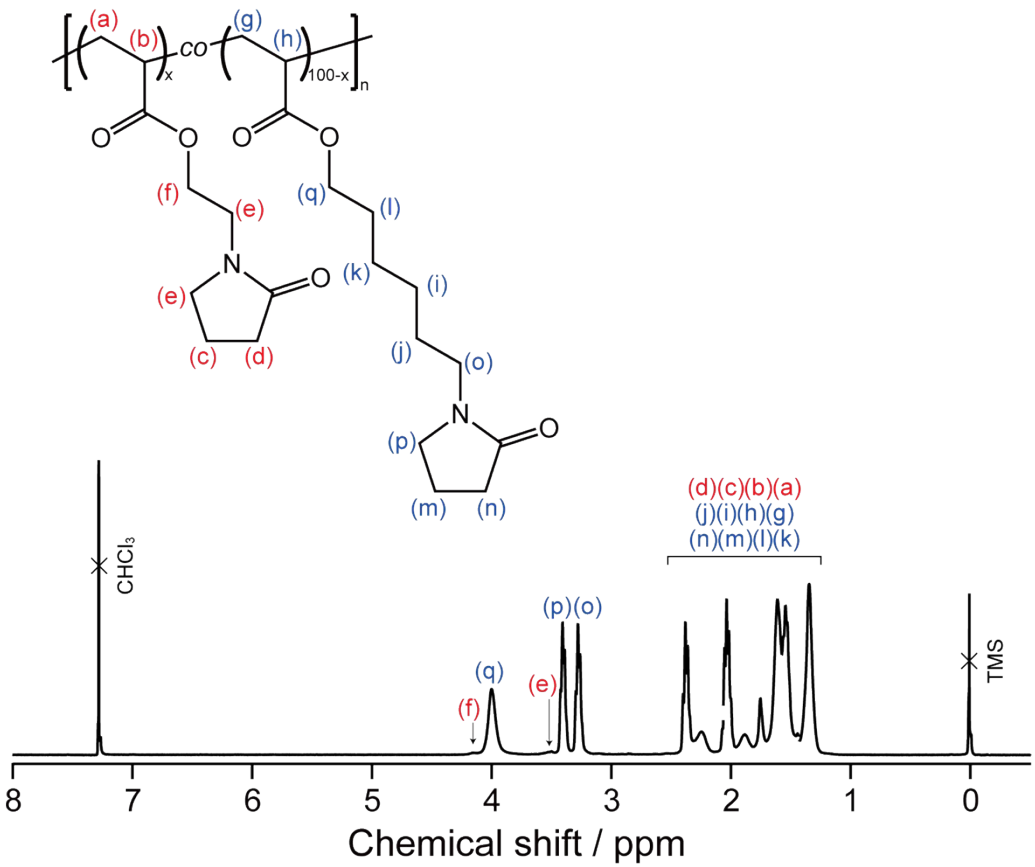

Figure S25. ^{1}H NMR spectrum of PNAEtP$_{3}$-*co*-PNAHxP$_{97}$ in chloroform-*d* at 25 °C.

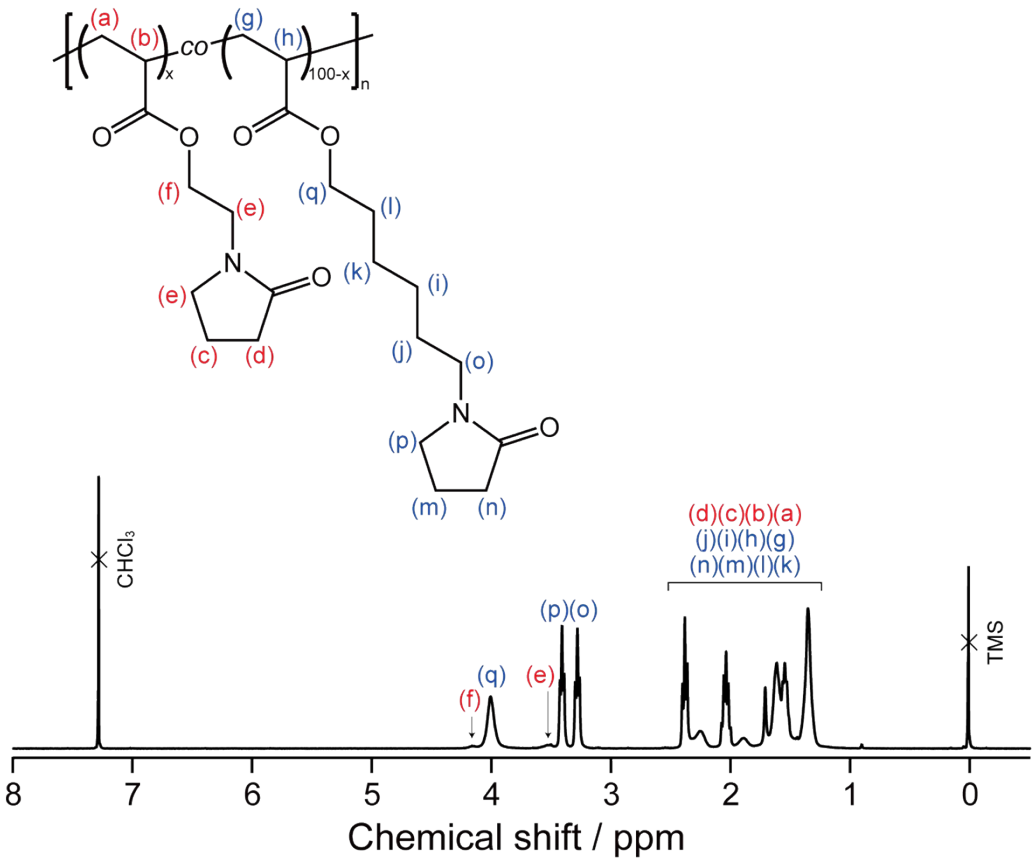

Figure S26. ^{1}H NMR spectrum of PNAEtP$_5$-*co*-PNAHxP$_{95}$ in chloroform-*d* at 25 °C.

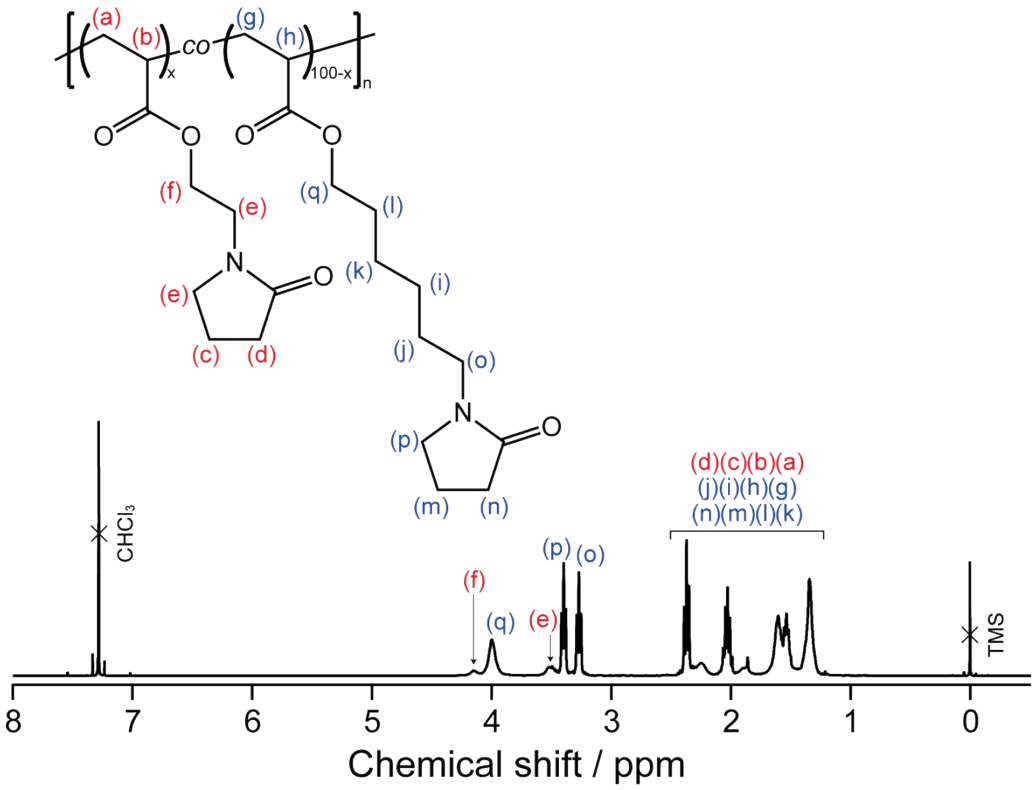

Figure S27. ^{1}H NMR spectrum of PNAEtP$_{10}$-*co*-PNAHxP$_{90}$ in chloroform-*d* at 25 °C.

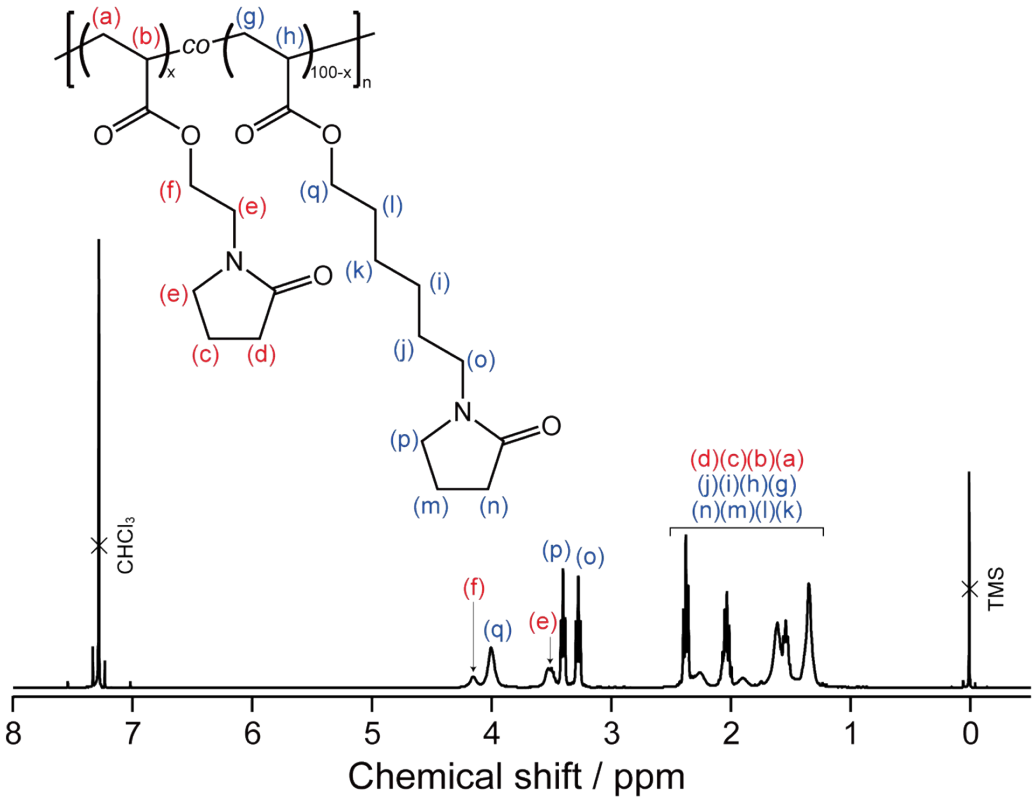

Figure S28. ^{1}H NMR spectrum of PNAEtP$_{20}$-*co*-PNAHxP$_{80}$ in chloroform-*d* at 25 °C.

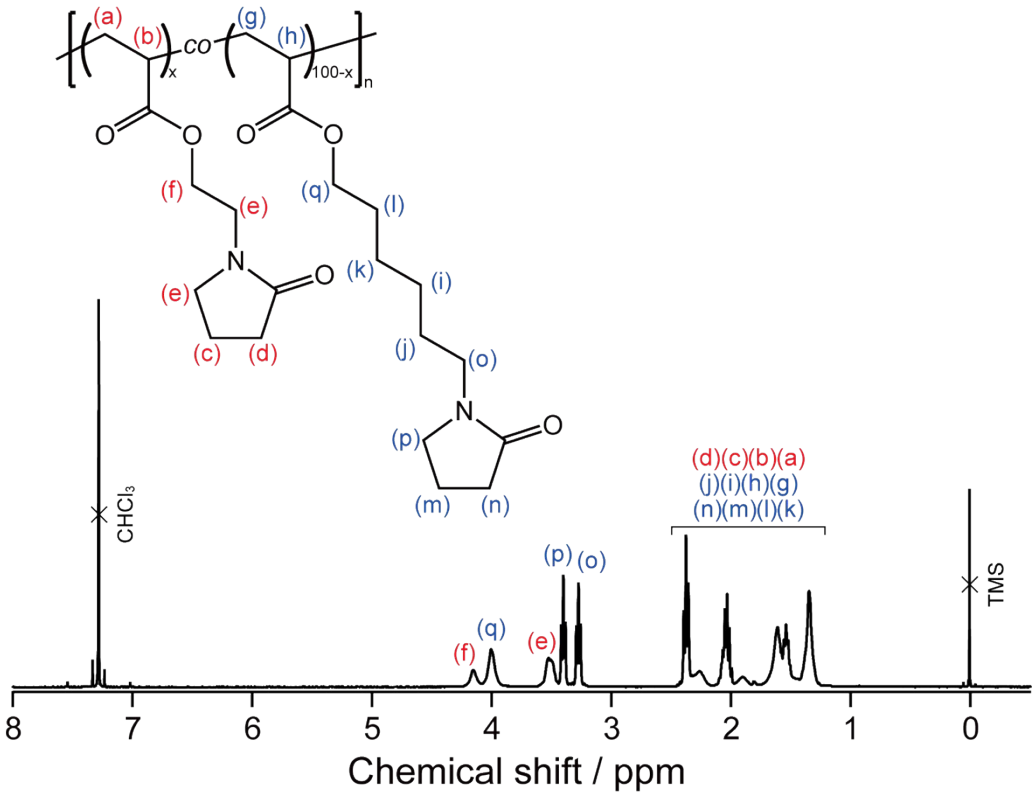

Figure S29. ^{1}H NMR spectrum of PNAEtP$_{30}$-*co*-PNAHxP$_{70}$ in chloroform-*d* at 25 °C.

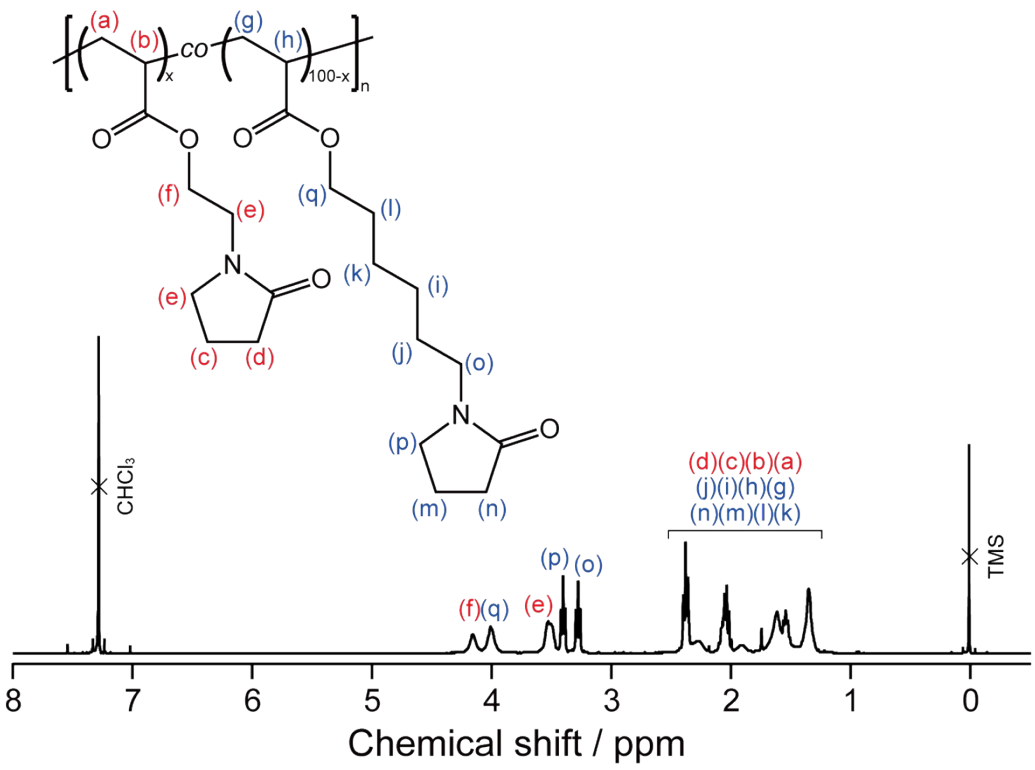

Figure S30. ^{1}H NMR spectrum of PNAEtP$_{40}$-*co*-PNAHxP$_{60}$ in chloroform-*d* at 25 °C.

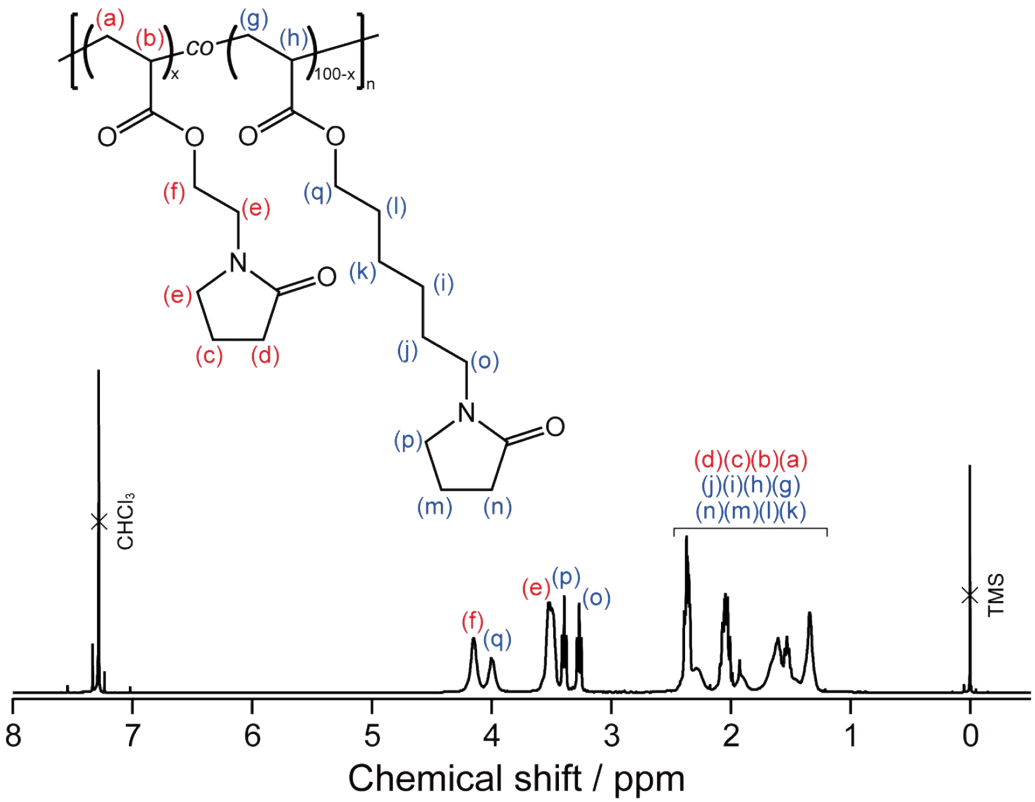

Figure S31. ^{1}H NMR spectrum of PNAEtP$_{60}$-*co*-PNAHxP$_{40}$ in chloroform-*d* at 25 °C.

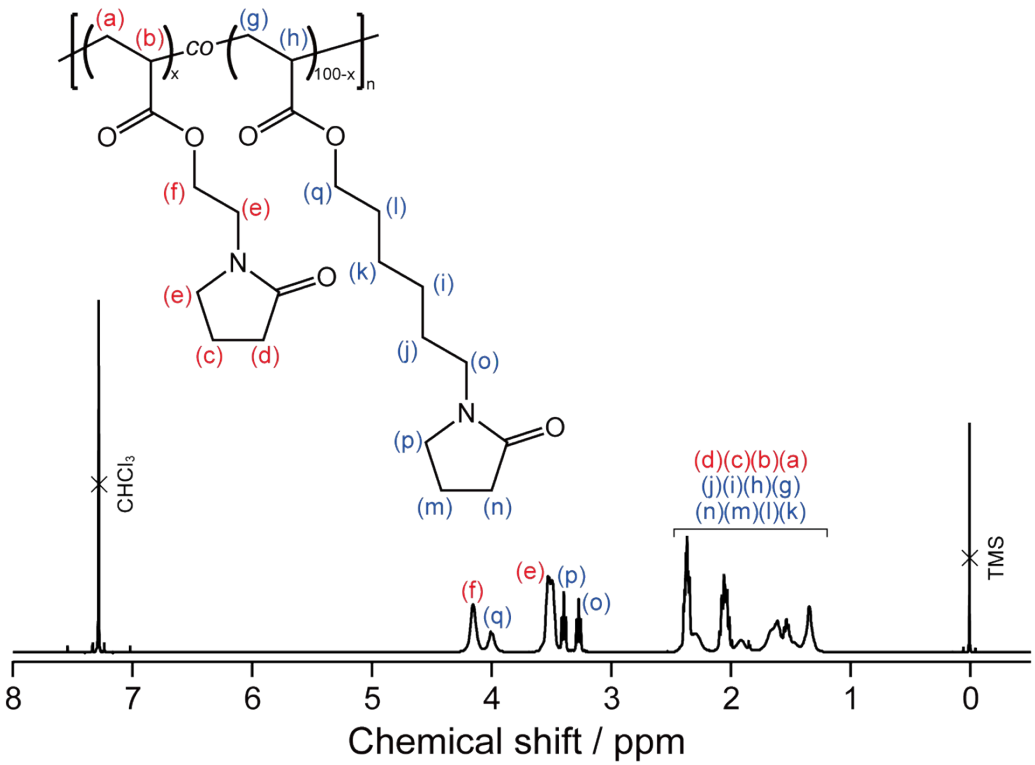

Figure S32. ^{1}H NMR spectrum of PNAEtP$_{70}$-*co*-PNAHxP$_{80}$ in chloroform-*d* at 25 °C.

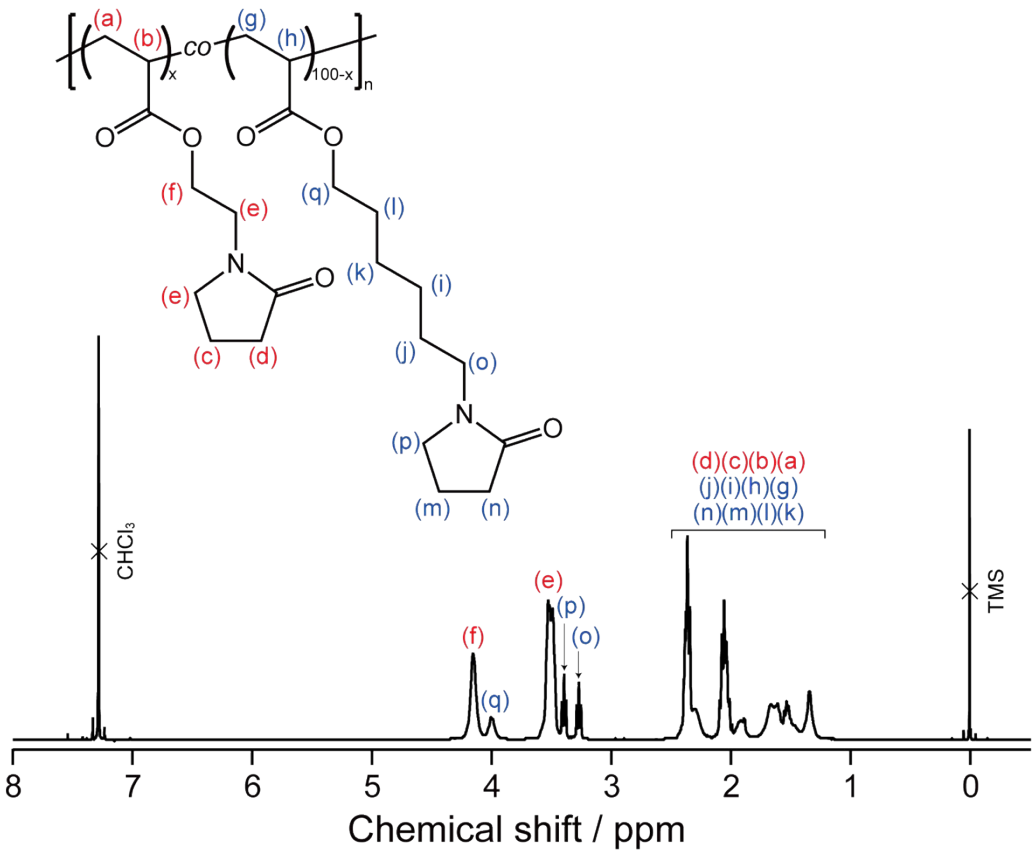

Figure S33. ^{1}H NMR spectrum of PNAEtP$_{80}$-*co*-PNAHxP$_{20}$ in chloroform-*d* at 25 °C.

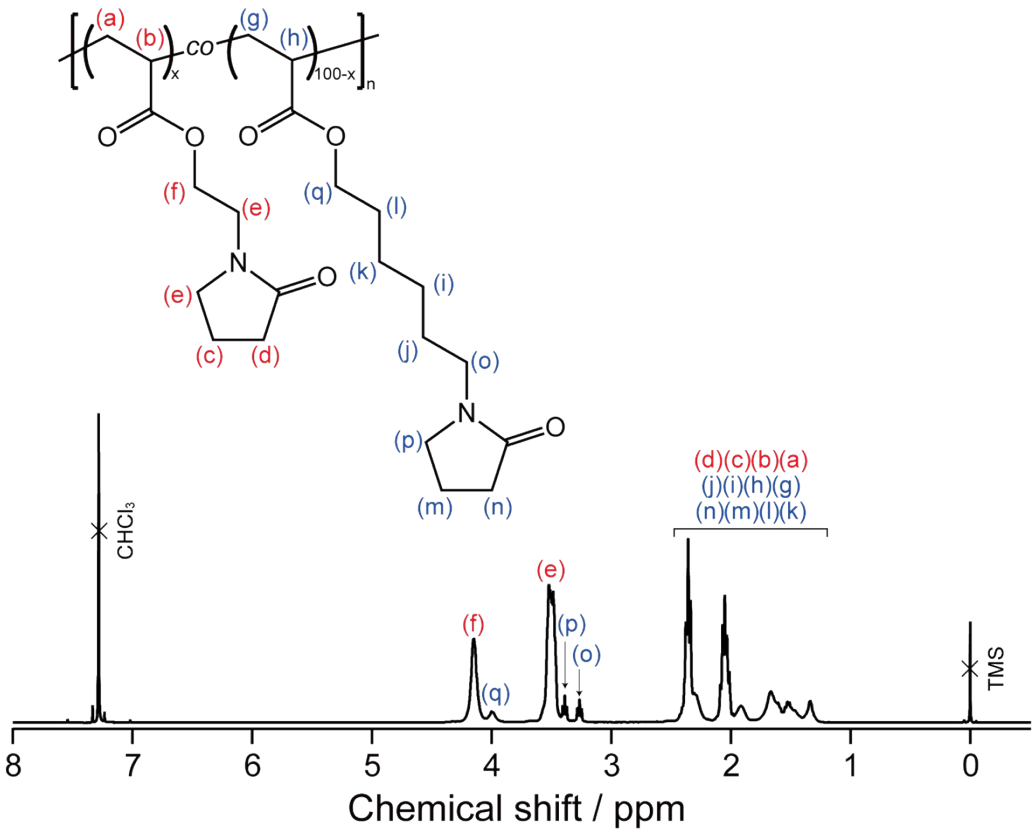

Figure S34. ^{1}H NMR spectrum of PNAEtP$_{90}$-*co*-PNAHxP$_{10}$ in chloroform-*d* at 25 °C.

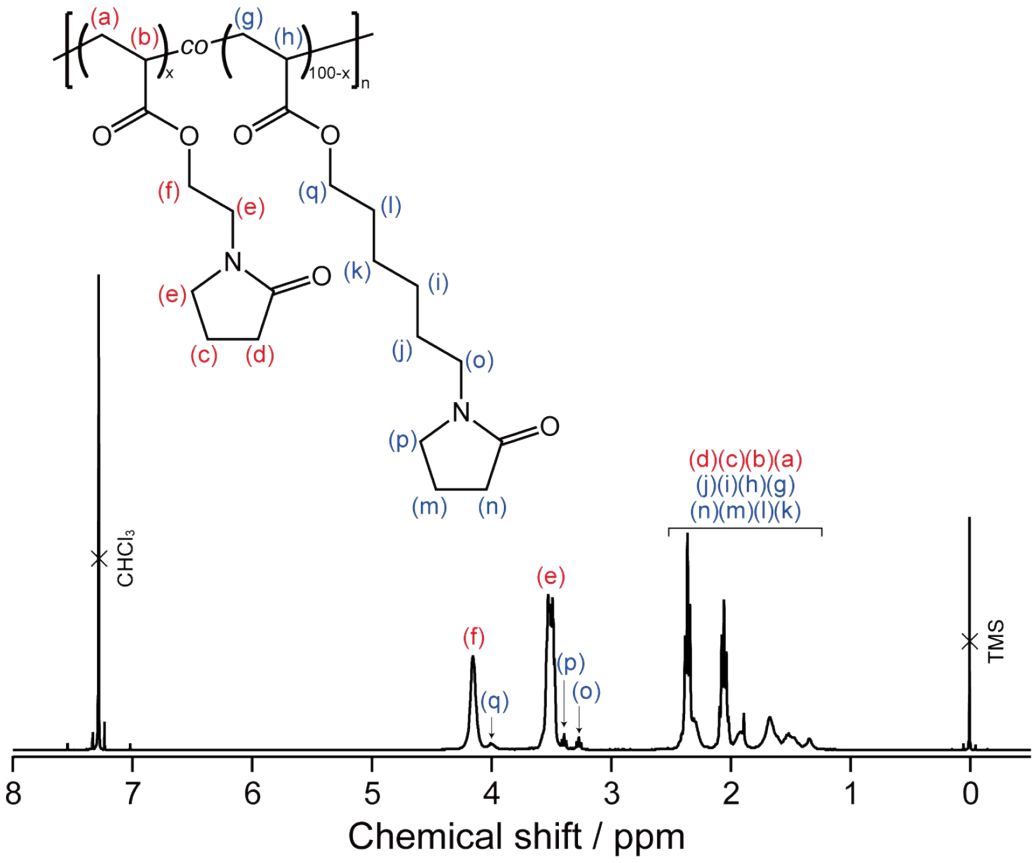

Figure S35. ^{1}H NMR spectrum of PNAEtP$_{95}$-*co*-PNAHxP$_{5}$ in chloroform-*d* at 25 °C.

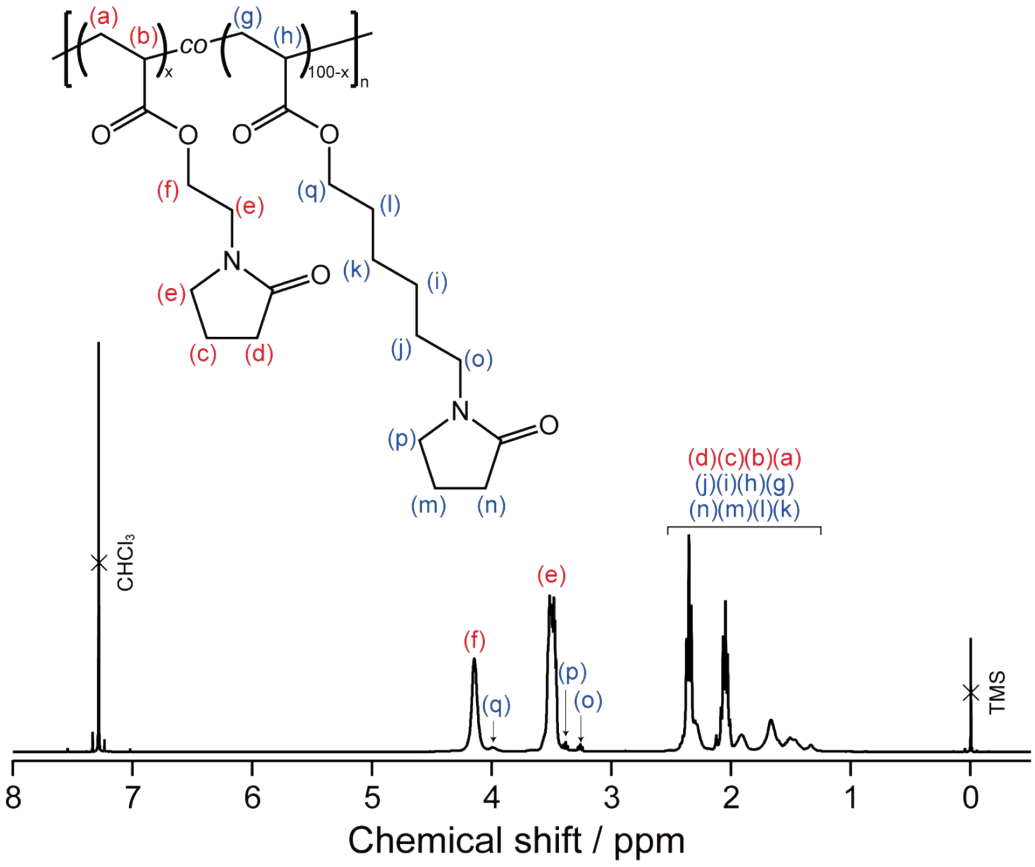

Figure S36. ^{1}H NMR spectrum of PNAEtP$_{97}$-*co*-PNAHxP$_{3}$ in chloroform-*d* at 25 °C.

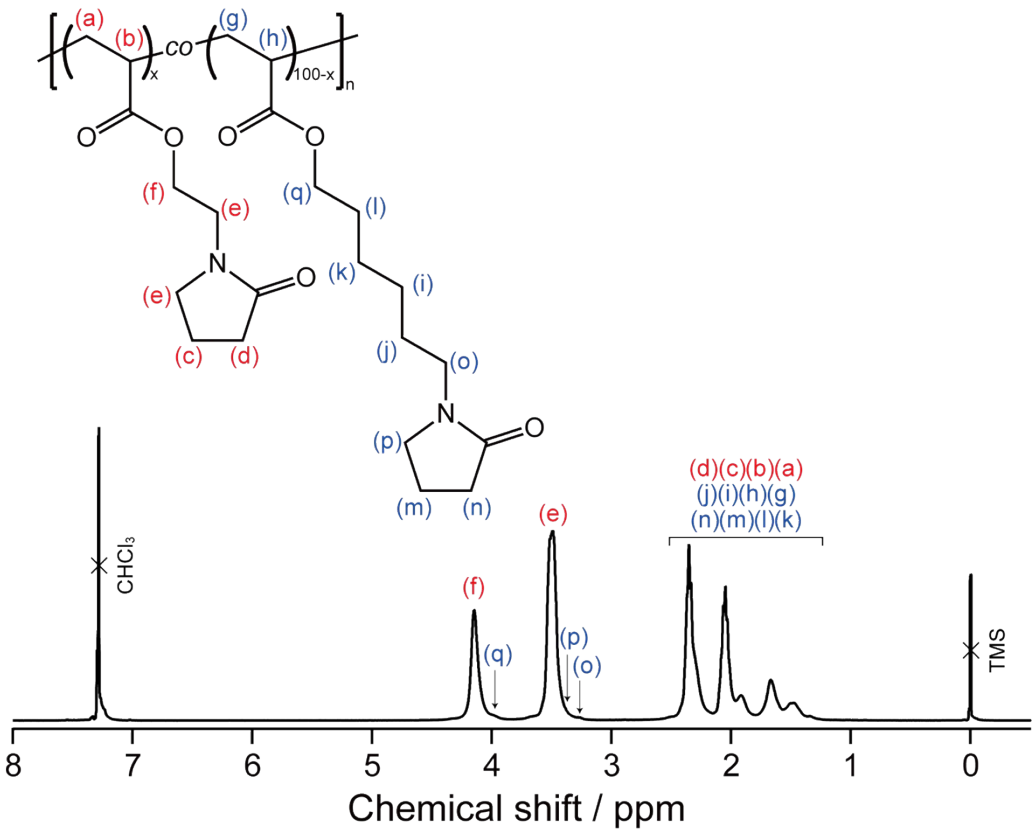

Figure S37. ^{1}H NMR spectrum of PNAEtP$_{99}$-*co*-PNAHxP$_{1}$ in chloroform-*d* at 25 °C.

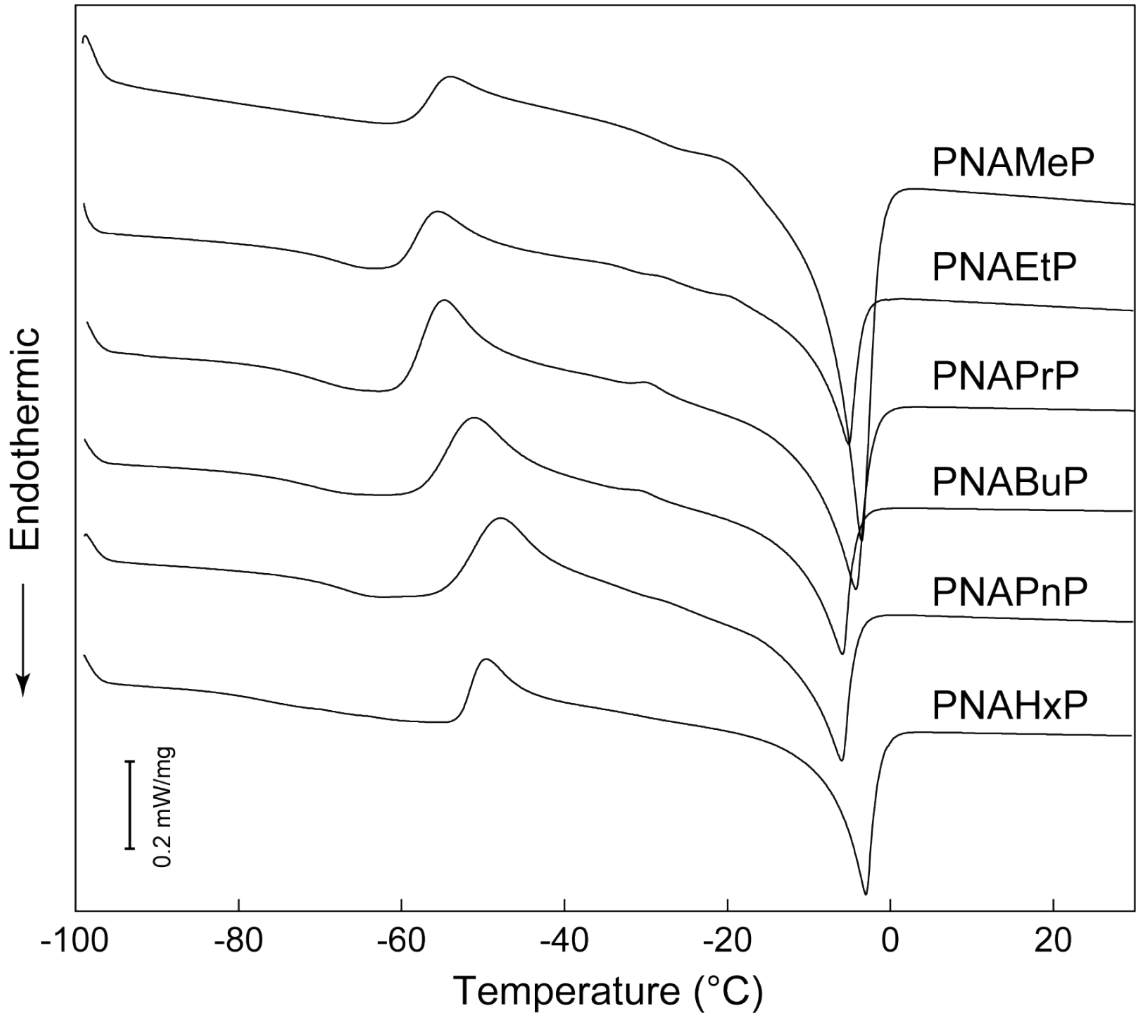

Figure S38. DSC thermograms of PNARPs under wet condition at a heating rate of 5 °C min^{-1}. The water contents for the polymers' samples were 41.3 wt% (PNAMeP), 39.2 wt% (PNAEtP), 38.8 wt% (PNAPrP), 39.6 wt% (PNABuP), 38.5 wt% (PNAPnP), and 39.0 wt% (PNAHxP).

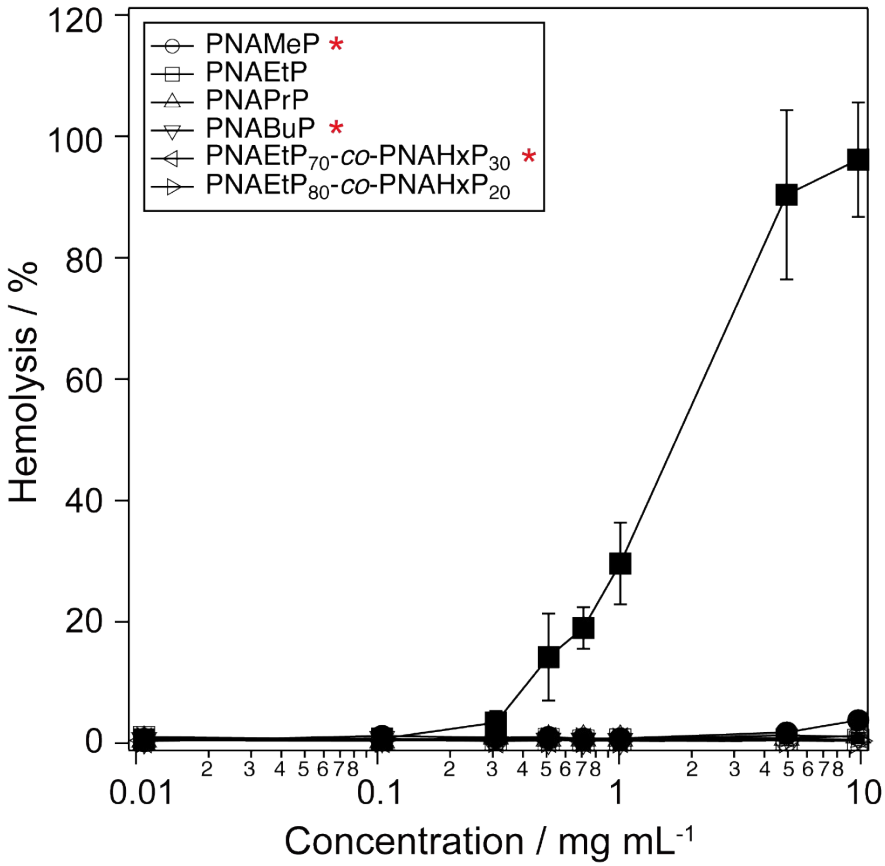

Figure S39. Hemolysis test of the (co)polymers at 20 °C. Red asterisk means the polymers having LCST below 37 °C.

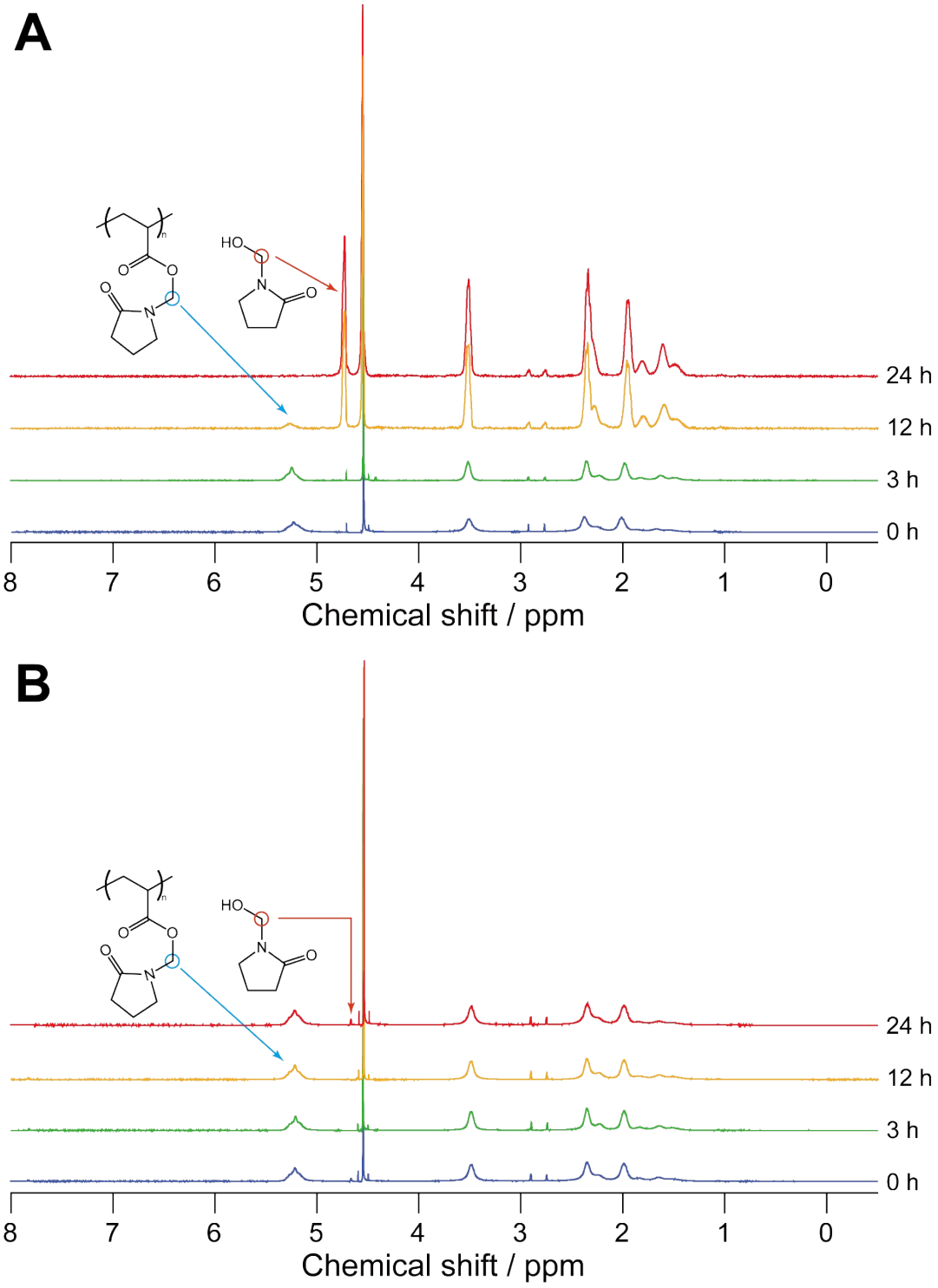

Figure S40. ^{1}H NMR spectra of PNAMeP in (A) deuterated-PBS and (B) deuterated-water containing 137 mM of sodium chloride and 2.7 mM potassium chloride at 37 °C. These spectra were collected after dissolution for 0, 3,

12, and 24 h.

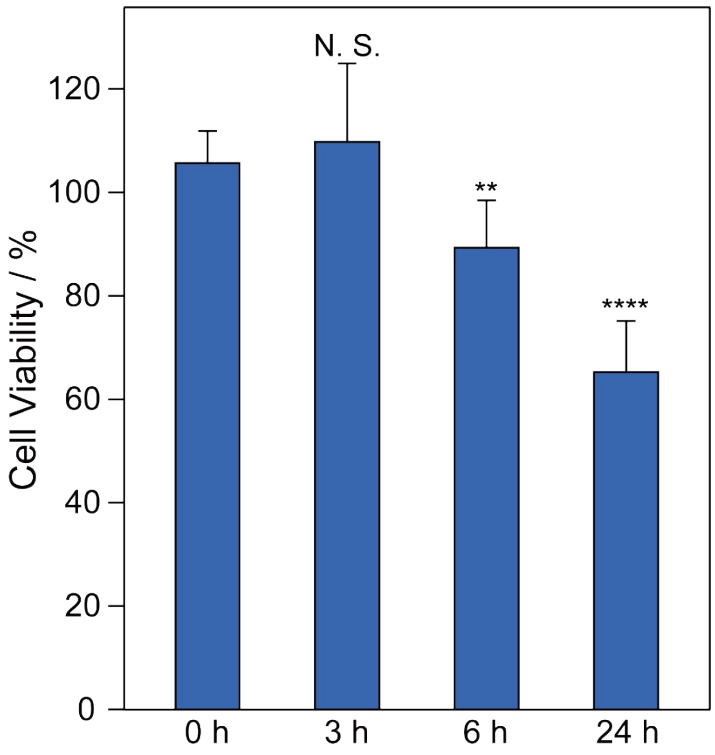

Figure S41. Viability of RAW264.7 after mixing with PNAMeP for 0, 3, 6, and 24 h. The cell density is equal to 1.0×10^4 cell well^{-1} (96 well plate). $^{**}p < 0.01$, $^{****}p < 0.001$, N. S. means not significant.

Table S1. Summary of the cloud point of PNABuP aqueous solutions with various polymer concentration.

Polymer concentration (%)	Cloud point, T_c (°C)
0.10	35.5
0.30	32.3
0.50	30.9
1.0	29.7
2.0	29.8
3.0	30.5
5.0	32.1
10.0	33.4
20.0	36.4
40.0	40.9

Table S2. Summary of the copolymerization of NARPs in this study.

P(NAR_1P_x-*co*-NAR_2P_{100-x})	Feed composition		Conv.[a] (%)	NAR_1P content (%)		M_n[b] (g mol^{-1})	$Đ$[b] (M_w/M_n)	$T_{g,\ dry}$[c] (°C)	LCST[d] (°C)
	NAR_1P (mmol)	NAR_2P (mmol)		Theoretical	Actual[a]				
P($NAMeP_{50}$-*co*-$NAPrP_{50}$)	3.00	3.00	88	50.0	50.0	41,500	1.91	12.3	47.9
P($NAPrP_{50}$-*co*-$NABuP_{50}$)	3.00	3.00	91	50.0	49.8	43,100	1.92	-11.3	42.2
P($NABuP_{50}$-*co*-$NAPnP_{50}$)	3.00	3.00	84	50.0	50.2	47,000	2.08	-21.6	13.1
P($NAEtP_{50}$-*co*-$NAHxP_{50}$)	3.00	3.00	86	50.0	50.0	41,300	1.89	-15.6	18.3

a) The conversion of monomers and composition of resultant polymers were evaluated by ^{1}H NMR analysis.

b) The number-average molecular weights and polydispersity indexes were calculated by SEC analysis (PMMA std.) in DMF (LiBr 10 mM) at 40 °C.

c) The glass transition temperatures were determined by DSC analysis (5 °C min^{-1}).

d) The LCSTs were determined by measuring transmittance at 600 nm (1 °C min^{-1}).