Articles

Copolymerization of Amino Acid Functionalized Norbornene Monomers. Synthesis of Amphiphilic Block Copolymers Forming Reverse Micelles

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ABSTRACT: Amino acid derived novel norbornene monomers, *N,N′*-(*exo*-bicyclo[2.2.1]hept-5-en-2,3-diyldicarbonyl) bis-L-leucine methyl ester (**1**) and *N,N′*-(*exo*-bicyclo[2.2.1]hept-5-en-2,3-diyldicarbonyl) bis-L-leucine (**2**) were synthesized and polymerized with Grubbs second generation ruthenium catalyst. The homopolymers, random, and block copolymers with number-average molecular weights ranging from 16 000 to 30 000 were obtained in good yields. The block copolymers with **1**:**2** unit ratios of 75:25, 62:38, and 50:50 were soluble in acetone, while the random copolymers with the same ratios were partly insoluble in the solvent. ^{1}H NMR, contact angle, dynamic light scattering, and atomic force microscopy measurements revealed that the block copolymer form micelles with a diameter around 100 nm in acetone consisting of a hydrophilic core of poly(**2**) and a hydrophobic shell of poly(**1**).

Introduction

The design and synthesis of highly ordered biologically functional polymers attract great interest. Amino acids and peptides are widely used as key components of synthetic biopolymers, because they are not only biologically relevant substances but also useful as highly pure chiral sources that possibly lead to new optically active biomimetic materials including controlled drug delivery systems, polyelectrolytes, and chiral recognition materials.[1−4] On the other hand, ring-opening metathesis polymerization (ROMP) of norbornene derivatives using well-defined transition metal catalysts allows a high level of control over many aspects of polymers such as molecular weights, polydispersities, backbone configurations, and tacticities.[5−8] Block copolymers with different functionalities are prepared via ROMP utilizing the living nature. Amphiphilic block copolymers are of interest because of their ability to self-assemble, forming nanoscale structures.[9−11] When a diblock copolymer is dissolved in a selective solvent, which is good for one block but poor for another one, it associates to form micelles.[12,13] Several attempts have been made regarding amino acid based amphiphile polymeric materials such as pH-sensitive amphiphile vesicles applicable to a drug delivery system,[14] protease-resistant amphiphilic diblock polypeptides applicable to catalysts and pharmaceuticals.[15,16]

Several research groups have synthesized diblock polymers consisting of 5-norbornene-2,3-dicarboxylic acid unit by ROMP, during which the carboxy groups are protected with trimethylsilyl[17−19] or *tert*-butyl groups,[20] and deprotected after isolating the formed copolymers. This protection-deprotection procedure is indispensable to synthesize well-defined carboxy-carrying ROMP-based block copolymers, because of intolerance of molybdenum catalysts to carboxy group,[19] or occurrence of side reactions with Grubbs catalysts preventing living polymerization.[20] The protection−deprotection of functional groups on polymers have drawbacks such as time and reagent loss, incomplete deprotection of the protected functional groups especially in the case of high-molecular-weight polymers.

We have previously reported that amino acid bifunctionalized norbornene derivatives efficiently undergo ROMP to give the polymers with fairly high molecular weights in good yields.[21,22] The polymerization proceeds in a living fashion to some extent. In the present study, we wish to report the successful synthesis of novel amino acid based norbornene block copolymers with ester and carboxy groups as hydrophobic and hydrophilic units, respectively, by direct copolymerization of ester monomer **1** and carboxylic acid monomer **2** using Grubbs second generation catalyst (Scheme 1). We also report the comparison of the amphihilicities between the block and random copolymers and micellization of the block copolymers.

Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded using tetramethylsilane (TMS) as an internal standard in $CDCl_3$ on a JEOL EX-400 spectrometer. IR and UV−vis spectra were measured on JASCO FTIR-4100 and V-550 spectrophotometers, respectively. Melting points (mp) were measured on a Yanaco micromelting point apparatus. Mass spectrum was measured on a JEOL JMS−HX110A mass spectrometer. Elemental analysis was done at the Microanalytical Center of Kyoto University. Number- and weight-average molecular weights (M_n and M_w) of polymers were determined by gel permeation chromatography (GPC) on a JASCO Gulliver system (PU-980, CO-965, RI-930, and UV-1570) equipped with polysty-

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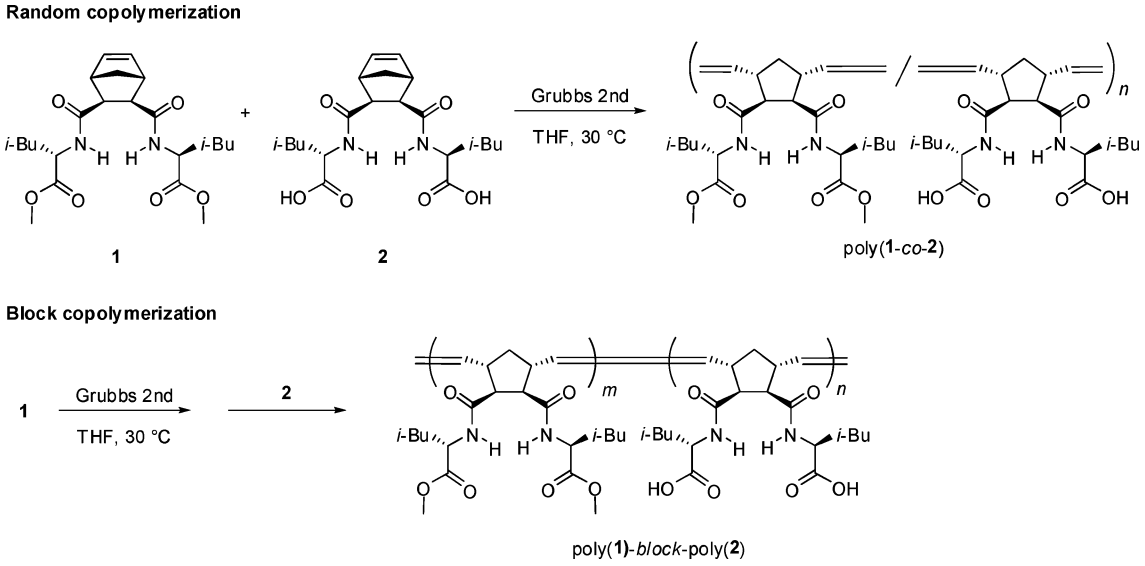
Scheme 1. Random and Block Copolymerizations of 1 with 2



rene gel columns (Shodex columns K804, K805, and J806), using tetrahydrofuran (THF) as an eluent at a flow rate of 1.0 mL/min, calibrated by polystyrene standards at 40 °C. Thermogravimetric analyses (TGA) were conducted in air with a Perkin-Elmer TGA7 thermal analyzer. Static contact angles of water on polymers that were spin-coated on glass plates from THF solutions were determined by the sessile-drop method using a Kyowa Interface Science CA-X contact angle meter at room temperature. A droplet of water (10 μL) was placed on a specimen for 30 s, and then a contact angle was measured. The measurement was repeated at 10 different positions on the same specimen, and these data were averaged. Dynamic light scattering (DLS) measurements were performed on a Viscotek 802DLS equipped with a 50 mW fiber coupled diode laser (830 nm), using omniSIZE 3.0 software. Atomic force microscopy (AFM) was performed on a Digital Instruments Multimode AFM controlled by a Nanoscope III scanning probe microscope controller.

Materials. Reagents were used as received unless stated otherwise. CH_2Cl_2 used for polymerization was distilled by the standard procedure before use.

Synthesis of *N,N′*-(*exo*-Bicyclo[2.2.1]hept-5-en-2,3-diyldicarbonyl) Bis-L-leucine Methyl Ester (1). *cis*-5-Norbornene-*exo*-2,3-dicarboxylic anhydride (2.05 g, 12.5 mmol) and L-leucine methyl ester hydrochloride (3.49 g, 25 mmol) were dissolved in CH_2Cl_2 (100 mL). Triethylamine (3.5 mL, 25 mmol) and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC·HCl, 2.39 g, 12.5 mmol) were added to the solution at 0 °C, and the resulting mixture was stirred at room temperature overnight. After that the mixture was subsequently washed with 1 M HCl(aq), saturated $NaHCO_3$(aq), and water twice, then dried over anhydrous $MgSO_4$. It was concentrated on a rotary evaporator to obtain **1** as white solid. Yield: 75%. Mp: 204−205 °C. $[\alpha]_D = -9.4°$ ($c = 0.1$ g/dL in $CHCl_3$, room temperature). IR (KBr): 3298 (N−H), 3064, 2957, 2870, 1755 (ester C═O), 1660 (amide C═O), 1555, 1469, 1448, 1369, 1328, 1301, 1256, 1234, 1209, 1169, 1149, 1055, 994, 736 cm^{-1}. ^1H NMR (400 Hz, $CDCl_3$): δ 0.92−0.95 (m, 12H, 4 × CH_3), 1.47−1.75 (m, 8H, 2 × CHCH$_3$, 2 × CH_2CH, norbornene CH_2), 2.46 (d, $J = 8.0$ Hz, 2H, 2 × CH), 3.01 (s, 2H, bridge position), 3.72 (s, 3H, COOCH_3), 3.73 (s, 3H, COOCH_3), 4.49−4.62 (m, 2H, 2 × >CHNH−), 6.00 (d, $J = 8.0$ Hz, 1H, −CONH−), 6.13 (d, $J = 8.0$ Hz, 2H, 2 × −CH═CH−), 6.22 (d, $J = 7.6$ Hz, 1H, −CONH−). ^{13}C NMR (100 Hz, $CDCl_3$): δ 22.13, 22.29, 22.60, 24.64, 24.71, 41.58, 41.83, 45.13, 45.59, 46.09, 48.47, 49.27, 50.71, 50.92, 52.12, 52.16, 138.23, 172.09, 173.61. Anal. Calcd for $C_{23}H_{36}N_2O_6$: C, 63.28; H, 8.31; N, 6.42. Found: C, 63.32; H, 8.12; N, 6.41.

Synthesis of *N,N′*-(*exo*-Bicyclo[2.2.1]hept-5-en-2,3-diyldicarbonyl) Bis-L-leucine (2). Monomer **1** (817 mg, 2 mmol) was dissolved in MeOH (15 mL). NaOH(aq) (2 M, 6 mL) was added to the solution at 0 °C, and the resulting mixture was stirred at room temperature overnight. A half amount of MeOH was removed on a rotary evaporator, and then the residue was acidified by the addition of 1 M HCl dropwise until the pH became ca. 3. After that, **2** was extracted from the mixture with ethyl acetate three times, and the combined organic phase was dried over anhydrous $MgSO_4$. It was concentrated on a rotary evaporator to obtain **2** as white solid. Yield: 80%. Mp: 179−180 °C. $[\alpha]_D = -5.9°$ ($c = 0.1$ g/dL in THF, room temperature). IR (KBr): 3316 (N−H), 3063, 2959, 2872, 2620, 1726 (carboxylic acid C═O), 1655 (amide C═O), 1541, 1470, 1451, 1369, 1327, 1301, 1264, 1240, 1208, 1170, 1154, 1046, 980, 728 cm^{-1}. ^1H NMR (400 Hz, DMSO-d_6): δ 0.79−0.88 (m, 12H, 4 × CH_3), 1.14−1.19 (m, 2H, 2 × CHCH$_3$), 1.31−1.63 (m, 6H, 2 × CH_2CH, norbornene CH_2), 2.33−2.42 (m, 2H, 2 × CH), 2.77 (s, 2H, bridge position), 4.21−4.27 (m, 2H, 2 × >CHNH−), 6.25 (d, $J = 8.0$ Hz 2H, 2 × −CH═CH−), 7.62−7.68 (m, 2H, −CONH−), 12.29 (s, broad, 2H, −COOH). ^{13}C NMR (100 Hz, DMSO-d_6): δ 21.57, 21.74, 22.74, 22.82, 23.92, 24.24, 41.23, 44.79, 45.57, 47.42, 50.01, 50.53, 138.04, 138.22, 171.72, 172.24, 173.86, 174.56. HRMS (FAB) $[M + H]^+$: calcd for $C_{21}H_{33}N_2O_6$, 409.233; found, 409.2331.

Homopolymerization of 1 and 2. Polymerizations were carried out in a glass tube equipped with a three-way stopcock under nitrogen. Monomer **1** (183 mg, 0.42 mmol) and Grubbs second generation Ru catalyst (3.6 mg, 4.2×10^{-3} mmol) were dissolved in CH_2Cl_2 (0.5 mL) separately. The catalyst solution was added to the monomer solution and the resulting mixture was vigorously stirred. It was kept in a water bath at 30 °C for 1 h, during which the color of the polymerization mixture gradually changed from pink to yellow. Then, ethyl vinyl ether was added to the mixture to quench the reaction. The mixture was poured into a large amount of hexane to precipitate a polymer. It was separated by filtration using a membrane filter (ADVANTEC H100A047A) and dried under reduced pressure. In the case of homopolymerization of **2**, THF was used as the solvent media for polymerization because it was insoluble in CH_2Cl_2. The monomer and catalyst concentrations were the same as those of the polymerization of **1**.

Spectroscopic Data of the Polymers. Poly(1). IR (KBr): 3398 (N−H), 2957, 2928, 1743 (ester C═O), 1655 (amide C═O), 1541,-1534, 1467, 1387, 1369, 1274, 1234, 1205, 1156, 1022, 981, 744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.87−0.90 (m, 12H, 4 × CH_3), 1.26−1.87 (m, 8H, 2 × CHCH$_3$, 2 × CH_2CH, norbornene CH_2), 2.61−2.79 (m, 2H, 2 × CH), 3.33 broad s, bridge position), 3.67−3.74 (m, 6H, 2 × COOCH_3), 4.54 (broad s, 2H, 2 × >CHNH−), 5.29−5.52 (broad, 2H, 2 × −CH═CH−), 6.43−6.49 (m, 2H, 2 × −CONH−).

Scheme 2. Synthesis of Monomers 1 and 2

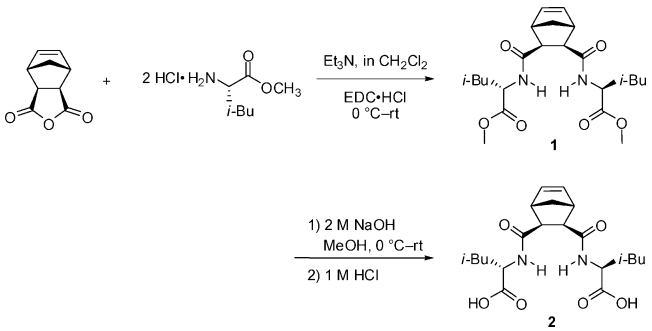


Table 1. Homo- and Copolymerizations of 1 and 2 [a]

feed ratio					unit ratio [e]		
1	**2**	yield[c] (%)	M_n[d]	M_w/M_n[d]	**1**	**2**	$[\alpha]_D$[f] (deg)
100[b]	0	93	16 000	1.20	100	0	−29.2
75	25	83	16 600	1.72	71	29	−7.7
50	50	96	23 000	1.67	53	47	−14.8
25	75	93	30 000	1.27	27	73	−13.4
0	100	89	26 000	1.54	0	100	−7.0

[a] Conditions: $[M]_{total}$ = 0.42 M in THF; catalyst Grubbs second generation; $[M]_{total}/[Ru]$ = 100; 30 °C; 1.5 h. [b] Polymerized in CH_2Cl_2. [c] Hexane-insoluble part. [d] Determined by GPC (THF, polystyrene calibration). [e] Determined by ^{1}H NMR (CD_3OD). [f] Measured by polarimetry (THF, c = 0.10 g/dL, room temperature).

Poly(2). IR (KBr): 3378 (N−H), 3066, 2958, 2873, 2615, 1724 (carboxylic acid C═O), 1654 (amide C═O), 1535, 1465, 1388, 1330, 1207, 1157, 1022, 860 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.83−0.90 (m, 12H, 4 × CH_3), 1.39−2.30 (m, 8H, 2 × CHCH$_3$, 2 × CH_2CH, norbornene CH$_2$), 2.49 (m, 2H, 2 × CH), 2.67 (s, 2H, bridge position), 3.98−4.06, 4.21 (broad, 2H, 2 × >CHNH−), 5.23 (broad, 2H, (2 × −CH═CH−), 7.47 (broad, s, 2H, −CONH−), 12.47 (s, broad, 2H, −COOH).

Random Copolymerization. It was carried out using monomer mixtures at set ratios in a manner similar to the homopolymerization. THF was used as a solvent.

Block Copolymerization. Monomer **1** was polymerized for 2−3 h in THF. A small portion was taken from the polymerization mixture of **1**, and subjected to ^{1}H NMR measurement to confirm the complete consumption of **1**. Monomer **2** was fed into the polymerization mixture, and the resulting mixture was further stirred for 24 h. The polymer was isolated in a manner similar to the homopolymerization.

Results and Discussion

Monomer Synthesis. Monomer **1** was synthesized by the reaction of 5-norbornene-*exo*,*exo*-dicarboxylic anhydride with 2 equiv of L-leucine methyl ester hydrochloride in 75% yield (Scheme 2). EDC·HCl was employed as a condensation agent because the urea derivative can be easily removed from the reaction mixture by washing with water.[21,22] Monomer **2** was synthesized by alkaline hydrolysis of **1** in 80% yields. The structures of the monomers were determined by IR and ^{1}H and ^{13}C NMR spectroscopies, besides elemental analysis and mass spectrometry.

Homo and Copolymerizations. The homo- and copolymerizations of **1** and **2** were carried out in THF using Grubbs second generation catalyst (1 mol %), which is tolerant to wide variety of functional groups including the carboxy group.[23−26] As listed in Table 1, monomers **1** and **2** satisfactorily underwent homopolymerization to produce polymers with molecular weights of 16 000 and 26 000, respectively. Judging from the relatively small polydispersity indices of the polymers (1.20 and 1.54), it is considered that the polymerization proceeded in a living fashion. Table 1 also lists the results of the copolymerization of **1** and **2** at different feed ratios. The copolymers with M_n's of 16 600−30 000 (M_w/M_n = 1.27−1.72) were obtained in high yields (83−96%).

Table 2. Block Copolymerization of 1 and 2 [a]

feed ratio					unit ratio[d]		
1	**2**	yield[b] (%)	M_n[c]	M_w/M_n[c]	**1**	**2**	$[\alpha]_D$[e] (deg)
75	25	76	18 400	1.31	78	22	−26.1
62	38	87	28 800	1.54	60	40	−25.4
50	50	89	21 600	1.54	53	47	−16.8
38	62	86	23 500	1.54	33	67	−14.3
25	75	80	23 500	1.58	32	68	−14.5

[a] Conditions: $[M]_{total}$ = 0.42 M in THF; catalyst Grubbs second generation; $[M]_{total}/[Ru]$ = 100; 30 °C; time, first stage 2−3 h and second stage 20−24 h. [b] Hexane-insoluble part. [c] Determined by GPC (THF, polystyrene calibration). [d] Determined by ^{1}H NMR (CD_3OD). [e] Measured by polarimetry (THF, c = 0.10 g/dL, room temperature).

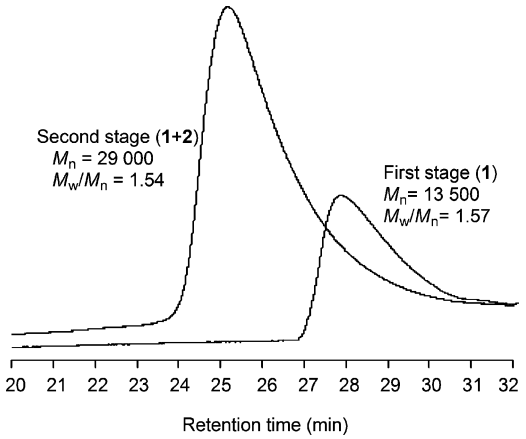


Figure 1. GPC traces of the first and second stages of block copolymerization (feed mole ratio of **1**:**2** = 62:38).

Block Copolymerization. Several attempts have been made to synthesize amphiphilic block copolymers of norbornene dicarboxylic acid with a hydrophobic norobornene derivative by ROMP. As described in the introduction, the carboxy groups are protected with bulky substituents such as *tert*-butyl[20] and trimethylsilyl[17,18] groups during the polymerization, and deprotected after isolation of block copolymers, because norbornene dicarboxylic acid does not afford a polymer with small polydispersity.

In the present study, monomer **2** with carboxy groups satisfactorily underwent ROMP to give a polymer with a relatively small polydispersity as listed in Table 1. The amino acid linker between norbornene and carboxy group seems to be effective to enhance the livingness of the polymerization. It is assumed that the linker prevents the carboxy group from interacting with a ruthenium center at the double bond in the metathesis intermediate. We therefore attempted the block copolymerization of **1** and **2** carrying carboxy groups without protection. In the first stage of the polymerization, monomer **1** was quantitatively converted within 3 h, which was confirmed by the ^{1}H NMR measurement of a sample portion drawn from the polymerization mixture. After that, monomer **2** was added to the mixture, and then the resulting mixture was stirred for another 24 h, leading to well-defined block copolymers with M_n's of 18 400−28 800 (M_w/M_n = 1.31−1.58) in high yields (76−89%) as listed in Table 2.[27] Figure 1 depicts the representative GPC chromatograms of the block copolymerization in the first and second stages. The chromatogram clearly shifted to a higher molecular weight region from the first stage to the second one keeping a unimodal distribution.

Table 3. Solubility of the Polymers [a]

	solvent									
polymer	hexane	toluene	CH_2Cl_2	$CHCl_3$	THF	acetone	DMF	DMSO	MeOH	NaOH aq (1 M)
poly(**1**)	−	±	+	+	+	+	+	+	+	−
poly(**2**)	−	−	−	−	+	−	+	+	+	+
poly(**1**-*co*-**2**)										
75:25	−	±	±	+	+	±	+	+	+	−
50:50	−	±	−	±	+	±	+	+	+	+
25:75	−	−	−	−	+	−	+	+	+	+
poly(**1**)-*block*-poly(**2**)										
75:25	−	±	±	+	+	+	+	+	+	+
62:38	−	±	±	±	+	+	+	+	+	+
50:50	−	±	±	±	+	+	+	+	+	+
38:62	−	±	−	±	+	±	+	+	+	+
25:75	−	±	−	−	+	−	+	+	+	+

[a] Key: (−) insoluble; (±) partly soluble; (+) soluble.

Table 3 lists the solubility of the homopolymers and copolymers. Both of the homopolymers, poly(**1**) and poly(**2**) were soluble in THF, DMF, DMSO, and MeOH. The copolymers were also completely soluble in these solvents irrespective of the copolymerization ratios. Meanwhile, poly(**1**) was soluble in CH_2Cl_2, $CHCl_3$, and acetone, while poly(**2**) was insoluble in these solvents. Consequently, it is predicted that the copolymers show solubility between the two homopolymers. Upon checking the solubility of the copolymers, we noticed an interesting difference in solubility between the random and block copolymers in acetone. Namely, the block copolymers with **1**:**2** unit ratios of 75:25, 62:38, and 50:50 were soluble in acetone, while the random copolymers with the same ratios were apparently partly insoluble in the solvent. Since the acetone solutions of block copolymers with **1**:**2** unit ratios of 62:38 and 50:50 were slightly turbid, it is assumed that they formed micelles. We examined the ^{1}H NMR spectra of the homo polymers and block copolymers to check the micelle formation. As shown in Figure 2, poly(**1**) and poly(**2**) exhibited signals reasonably assignable to the structures with the proper integration ratios in acetone-d_6 and DMSO-d_6, respectively. On the other hand, the block copolymer exhibited a methyl ester proton signal at 3.7 ppm and a carboxy proton signal at 12.5 ppm in DMSO-d_6 as shown in Figure 3. In acetone-d_6, it exhibited a methyl ester proton signal but no carboxylic acid one at all. When block copolymers form micelles, the integration ratio of ^{1}H NMR signals of the core part commonly becomes smaller than the calculated one, or sometimes becomes negligible.[20] Consequently, it is suggested that the absence of carboxylic acid proton in acetone-d_6 is caused by the formation of a reverse micelle consisting of a core of poly(**2**) and a shell of poly(**1**).[28]

To obtain further information on the amphiphilic property of the copolymers, we measured the static contact angles of water on the copolymers spin-coated on glass plates. Figure 4 plots the contact angles as a function of unit ratio of **1** in the block and random copolymers. The block copolymers exhibited contact angles 8−15° larger than those of the random copolymers irrespective of the monomer unit ratios. This result indicates that the hydrophobic block consisting of monomer unit **1** preferably exists in the near-surface region, presumably because the hydrophilic block consisting of monomer unit **2** preferably exits at the interface between the polymer phase and glass, due to the hydrophilicity of the glass surface. Both of the block and random copolymers with a higher content of monomer unit **1** displayed a larger contact angle. An increase of monomer **1** unit in the copolymers led to an increase of hydrophobicity of the copolymers.

Characterization of Reverse Micelle. Turbidity is a simple and convenient index to detect aggregates, because it reflects

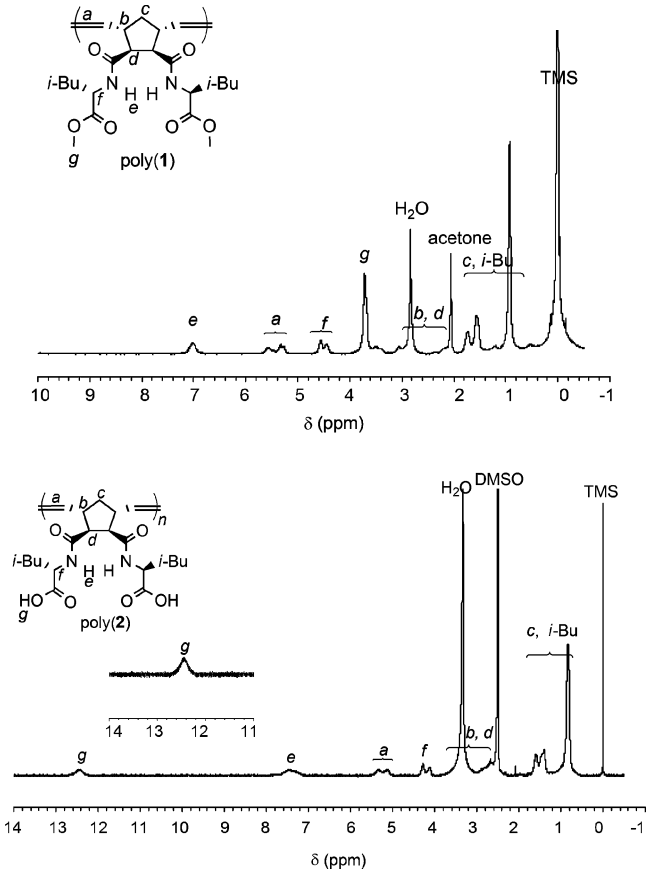


Figure 2. ^{1}H NMR spectra (400 MHz) of poly(**1**) measured in acetone-d_6 and poly(**2**) measured in DMSO-d_6.

the change in size of particles dispersed in solution.[29] Several reports use turbidity to determine the micelle formation, lower critical solution temperature, micelle stability, and critical water concentration.[30−33] In the present study, we measured the turbidity of polymer solutions by UV−vis spectroscopy. Figure 5 shows the transmittance of 1 wt % solutions of poly(**1**)-*block*-poly(**2**) (50:50) in THF, NaOH aq (1 M), and acetone. THF is a good solvent that dissolves both hydrophilic and hydrophobic blocks as listed in Table 3. Acetone is a solvent for reverse micelle formation as described above, and NaOH(aq) is considered to be a solvent for formation of micelles consisting of a core of **1** and a shell of **2**, judging from the solubility data listed in Table 3. The transmittance of the polymer solutions in acetone and NaOH(aq) at 400−700 nm was lower than that in THF, which indicates that larger size molecules (micelles) exist in the former two solvents. The transmittance of the polymer solution in NaOH(aq) became higher after 6 days. It is assumed

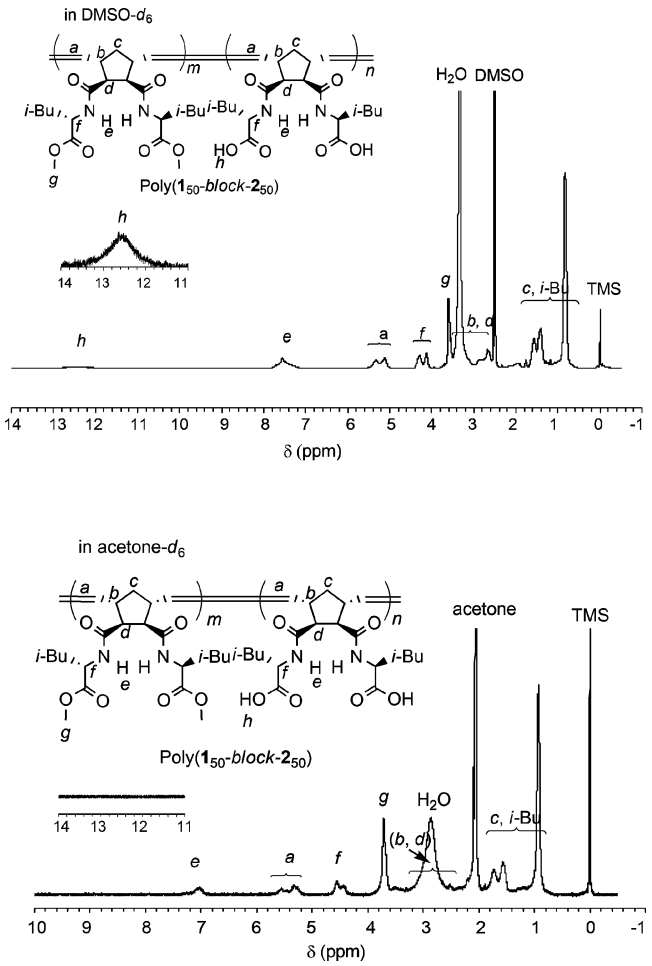


Figure 3. ^{1}H NMR spectra (400 MHz) of poly(**1**)-*block*-poly(**2**) (50:50) measured in DMSO-d_6 and acetone-d_6.

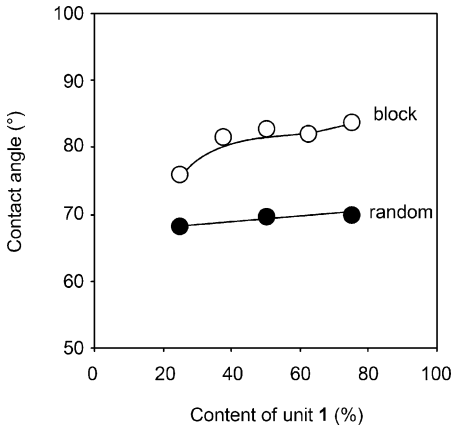


Figure 4. Contact angles of water on the random and block copolymers of **1** and **2** spin-coated from THF solutions on a glass plate as a function of monomer unit content of **1**.

that the methyl ester moieties of the copolymer gradually underwent hydrolysis, leading to transformation of micelles into unimers. In fact, we confirmed the ester hydrolysis by ^{1}H NMR measurement in a solution of NaOD in D_2O. Namely, the methyl ester proton signal gradually decreased and a peak assignable to methanol appeared at 3.4 ppm.

The critical micelle concentration (cmc) is defined phenomenologically from sharp changes in measurable quantities, which occur in a concentration range close to cmc. Many physical properties exhibit abrupt changes at cmc such as turbidity, solubilization and surface tension.[34] In the present study, we

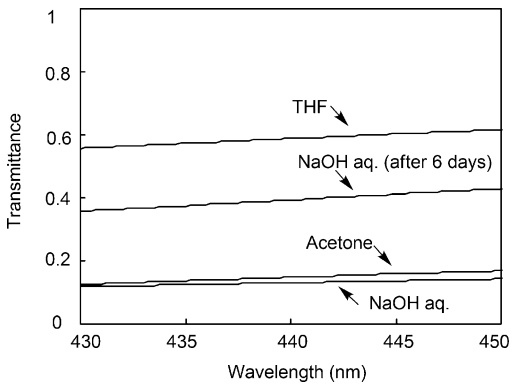


Figure 5. Transmittance of poly(**1**)-*block*-poly(**2**) (50:50) solution (c = 1 wt %) in THF, NaOH(aq) (1 M), and acetone.

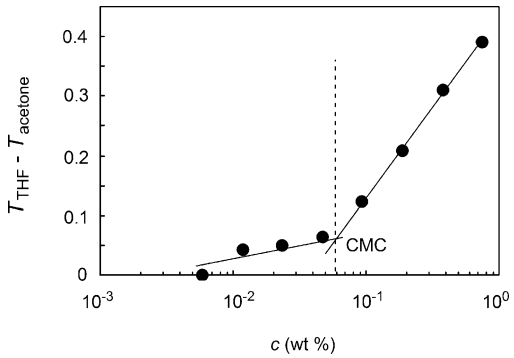


Figure 6. Difference between the transmittance (T) of THF and acetone solutions of poly(**1**)-*block*-poly(**2**) (50:50) at 435 nm vs concentration.

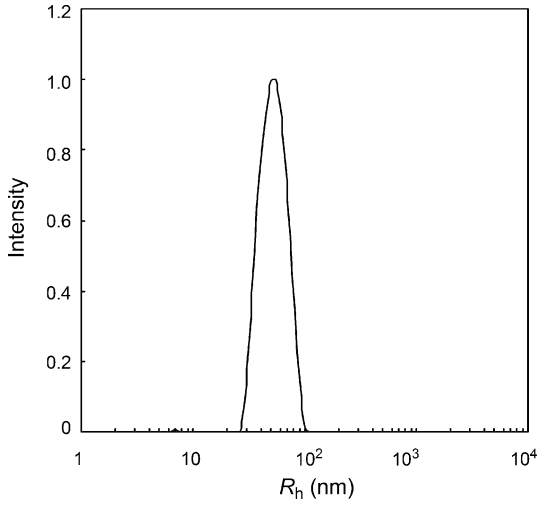


Figure 7. Distribution of particle size (R_h: hydrodynamic radius) of poly(**1**)-*block*-poly(**2**) (50:50) solution in acetone (1 wt %) measured by dynamic light scattering.

determined the cmc of poly(**1**)-*block*-poly(**2**) (50:50) in acetone using turbidity as the physical property. Figure 6 plots the relationship between the turbidity and concentration of poly(**1**)-*block*-poly(**2**) (50:50) in acetone, wherein the turbidity is defined by the difference of transmittance at 435 nm between in THF and acetone. It clearly showed a turning point around $c = 5 \times 10^{-2}$ wt %, which could be regarded as the cmc.

As described above, ^{1}H NMR spectroscopic and transmittance measurements indicated that the diblock copolymer formed reverse micelles in acetone. We performed dynamic light scattering (DLS) to confirm the micelle formation. As depicted in Figure 7, the presence of particles with an average hydrodynamic radius (R_h) around 50 nm was confirmed in a solution of poly(**1**)-*block*-poly(**2**) (50:50). The particles are considered

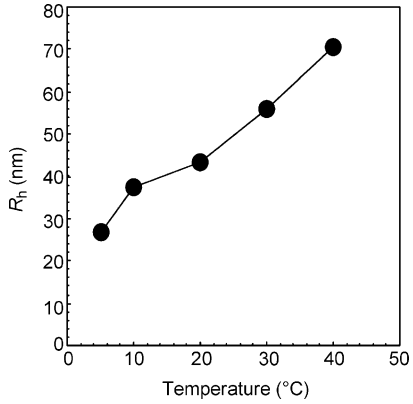


Figure 8. Hydrodynamic radius (R_h) of poly(**1**)-*block*-poly(**2**) (50:50), (c = 1 wt %) as a function of temperature measured in acetone.

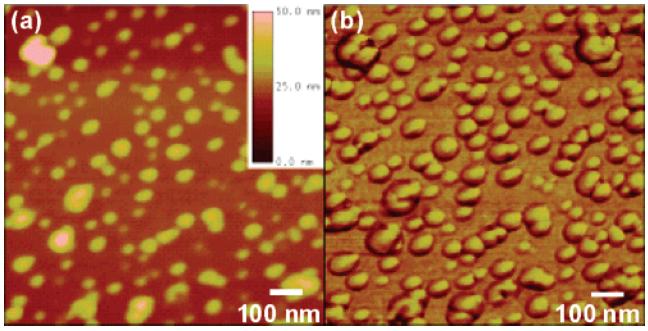


Figure 9. AFM (a) height image and (b) phase image of poly(**1**)-*block*-poly(**2**) (50:50) micelle adsorbed onto a silicon wafer from an acetone solution ($c = 5.86 \times 10^{-3}$ wt %).

to be aggregates, i.e., micelles in this case, because no such large size particles but R_h around 10 nm were observed in THF.

In addition, the temperature effect on the R_h of the micelle of poly(**1**)-*block*-poly(**2**) (50:50) at 0.19−1 wt % in acetone was investigated at 5−40 °C as shown in Figure 8. The R_h increased by raising temperature, as commonly observed due to expansion and loosening of micelle structures;[35] the molecular vibrations and translational motions increase by raising the temperature.

We further investigated the morphology of the reverse micelle by atomic force spectroscopy (AFM). The sample was fabricated by dropping a copolymer solution in acetone onto a silicon substrate. Spherical shapes with diameters mainly around 80−100 nm were clearly observed by AFM as shown in Figure 9, which was in good agreement with the size distribution determined by the DLS measurement (R_h 50 nm). Spheres larger than 100 nm seem to be aggregates of some micelles.

The thermal stability of the homopolymers and copolymers was studied by TGA measurement as shown in Figure 10. The temperature at 10% weight loss decreased as the content of unit **2** increased. The incorporation of monomer unit **2** made the copolymer thermally unstable, presumably due to decarboxylation. We also analyzed the polymers by DSC, but found no glass transition and melting temperatures up to 200 °C.

Conclusions

In this article, we have demonstrated the synthesis and ROMP of amino acids-derived novel hydrophobic and hydrophilic norbornene monomers, **1** and **2**. The homo, random, and block copolymerizations using Grubbs second generation catalyst satisfactorily proceeded to give the corresponding polymers in good yields. No protection of carboxy groups of **2** was necessary during ROMP to obtain well-defined block copolymers. The hydrophobicity of the copolymers increased with increasing

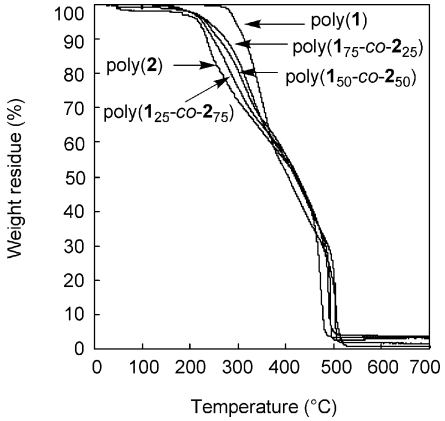


Figure 10. TGA curves of the polymers.

monomer unit **1**. The block copolymers formed reverse micelles in acetone, consisting of a hydrophilic core of poly(**2**) and a hydrophobic shell of poly(**1**). The diameter of the micelles was around 100 nm, which was confirmed by both DLS and AFM measurements.

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Supporting Information Available: Conversion−time relationships of monomers **1** and **2** (Figure S1). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Biagini, S. C. G.; Coles, M. P.; Gibson, V. C.; Giles, M. R.; Marshall, E. L.; North, M. *Polymer* **1998**, *39*, 1007−1014.
(2) Maynard, H. D.; Okada, S. Y.; Grubbs, R. H. *Macromolecules* **2000**, *33*, 6239−6248.
(3) Maynard, H. D.; Okada, S. Y.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 1275−1279.
(4) Sanda, F.; Endo, T. *Macromol. Chem. Phys.* **1999**, *200*, 2651−2661.
(5) Grubbs, R. H.; Tumas, W. *Science* **1989**, *243*, 907−915.
(6) Schrock, R. R. *Acc. Chem. Res.* **1990**, *23*, 158−165.
(7) Bazan, G. C.; Shrock, R. R.; Khosravi, E.; Feast, W. J.; Gibson, V. C.; O'Regan, M. B.; Tomas, J. K.; Davis, W. M. *J. Am. Chem. Soc.* **1990**, *112*, 8378−8387.
(8) Feast, W. J.; Gibson, V. C.; Marshall, E. L. *J. Chem. Soc., Chem. Commun.* **1992**, 1157−1158.
(9) Lodge, T. P. *Macromol, Chem. Phys.* **2003**, *204*, 265−273.
(10) Froster, S.; Plantenberg, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 689−714.
(11) Hamley, I. W.; Castelletto, V. *Prog. Polym. Sci.* **2004**, *29*, 909−948.
(12) Gohy, J. F. *Adv. Polym. Sci.* **2005**, *190*, 65−136.
(13) Rodriguez-Hernandez, J.; Checot, F.; Gnanou, Y.; Lecommandoux, S. *Prog. Polym. Sci.* **2005**, *30*, 691−724.
(14) Wang, C.; Huang, J.; Tang, S.; Zhu, B. *Langmuir* **2001**, *17*, 6389−6392.
(15) Xu, H.; Gall, N. L.; Jia, L. *ACS Polym. Prepr.* **2004**, *45* (2), 624−625.
(16) Li, B. S.; Cheuk, K. K. L.; Yang, D.; Lam, J. W. Y.; Wan, L. J.; Bai, C.; Tang, B. Z. *Macromolecules* **2003**, *36*, 5447−5450.
(17) Ahmed, S. R.; Bullock, S. E.; Cresce, A. V.; Kofinas, P. *Polymer* **2003**, *44*, 4943−4948.
(18) Ahmed, S. R.; Kofinas, P. *Macromolecules* **2002**, *35*, 3338−3341.
(19) Saunders, R. S.; Cohen, R. E.; Wong, S. J.; Schrock, R. R. *Macromolecules* **1992**, *25*, 2055−2057.
(20) Stubenrauch, K.; Moitzi, C.; Fritz, G.; Glatter, O.; Trimmel, G.; Stelzer, F. *Macromolecules* **2006**, *39*, 5865−5874.

(21) Sutthasupa, S.; Terada, K.; Sanda, F.; Masuda, T. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5337−5343.
(22) Sutthasupa, S.; Terada, K.; Sanda, F.; Masuda, T. *Polymer* **2007**, *48*, 3026−3032.
(23) Kiessling, L. L.; Owen, R. M. In In *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, Germany, 2003; Vol. 3; Chapter 3.6.
(24) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953−956.
(25) Choi, T-L.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 1743−1746.
(26) Romero, P. E.; Piers, W. E.; Mcdonald, R. *Angew. Chem., Int. Ed.* **2004**, *43*, 6161−6165.
(27) We polymerized monomer **1** first and then **2** in the synthesis of block copolymers, because we thought that the carboxylic acid moieties of monomer **2** might interact with the catalyst to retard the polymerization as described in the Introduction. If this occurs, the order in the present study is better than that of **2** first and then **1** for obtaining the block copolymer more efficiently, because the quantitative conversion of the first monomer is important. In fact, the rate of polymerization of monomer **1** was higher than that of **2** (see Supporting Information).
(28) This may be also brought about by the exchange between the carboxylic acid proton and acetone-d_6. If poly(**2**) was soluble in acetone-d_6, we could determine the H/D exchange rate and discuss the possibility much more.
(29) Bakshi, M. S.; Singh, J.; Singh, K.; Kaur, G. *Colloids Surf. A: Physicochem. Eng. Asp.* **2004**, *237*, 61−71.
(30) Zhang, J. X.; Qiu, L. Y.; Jin, Y.; Zhu, K. J. *Colloids Surf. B: Biointerfaces* **2005**, *43*, 123−130.
(31) Huang, C. J.; Shieu, F. S. *Colloid Polym. Sci.* **2005**, *284*, 192−202.
(32) Halacheva, S.; Rangelov, S.; Tsvetanov, C. *Macromolecules* **2006**, *39*, 6845−6852.
(33) Lee, E. S.; Shin, H. J.; Na, K.; Bae, Y. H. *J. Controlled Release* **2003**, *90*, 363−374.
(34) Hamley, I. W. In *Introduction to Soft Matter: Polymers, Colloids, Amphiphiles and Liquid Crystals*; Wiley-VCH: Weinheim, Germany, 2000; Chapter 4.6, page 217.
(35) Liaw, D. J.; Huang, C. C.; Kang, E. T. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 2901−2911.

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