Syntheses and Radical Polymerization Behavior of Methacrylamides Having Peptide Moieties: Effect of the Methylene Chain Introduced between the Methacrylamide and Peptide Moieties on the Polymerizability and Polymer Structure

Hironobu Murata, Fumio Sanda, and Takeshi Endo*

Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta-cho, Midori-ku, Yokohama 226, Japan

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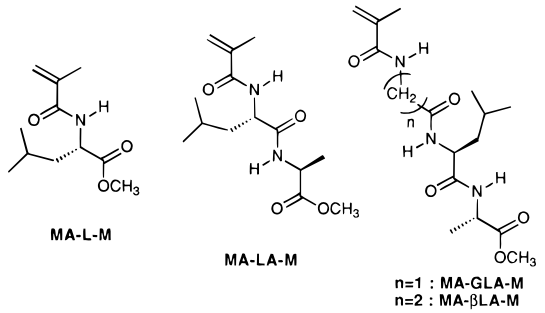
ABSTRACT: Syntheses and radical polymerization behavior of methacrylamides having peptide moieties, *N*-(methacryloylglycyl)-L-leucyl-L-alanine methyl ester (MA-GLA-M) and *N*-(methacryloyl-*β*-alanyl)-L-leucyl-L-alanine methyl ester (MA-*β*LA-M), were examined. Radical polymerizations of MA-GLA-M and MA-*β*LA-M in the presence of AIBN (1 mol %) in DMF (1.0 mol/L) afforded the corresponding polymers (poly(MA-GLA-M) and poly(MA-*β*LA-M)) in nearly quantitative conversions with $\overline{M}_{ns}$ 68 000 and 69 000, respectively. An increase of the absolute value of molecular rotation on the transformation from MA-GLA-M (−126.0°) and MA-*β*LA-M (−132.9°) to poly(MA-GLA-M) (−176.5°) and poly(MA-*β*LA-M) (−242.1°) could be observed. The radical polymerizability of MA-*β*LA-M in MeOH was suggested to be lower than that of MA-GLA-M. The CD patterns of poly(MA-GLA-M) and poly(MA-*β*LA-M) were similar to those of the corresponding model compounds.

Introduction

Several optically active polymers have been synthesized, and their applications to chromatographic resolution[1] and chiral induction[2] have been examined. We have developed amino acids and peptides as chemical functional materials as well as optical and biocompatible materials.[3] We have already reported synthesis and radical polymerization of a methacrylamide having a L-leucine methyl ester structure, *N*-methacryloyl-L-leucine methyl ester (MA-L-M).[4] Radical polymerization behavior of MA-L-M was unique and interesting. Namely, both inversion and increase of the absolute value of the specific rotation from MA-L-M to poly(MA-L-M) could be observed. The monomer reactivity ratio of MA-L-M was larger than that of methyl methacrylate and different from the usual methacrylamides. Recently, we have reported that a methacrylamide having a L-leucyl-L-alanine methyl ester structure, *N*-methacryloyl-L-leucyl-L-alanine methyl ester (MA-LA-M), shows higher radical polymerizability than MA-L-M, and a large increase of the absolute value of the specific rotation can be observed in the transformation from the monomer to polymer.[5] Since the side chains of MA-LA-M more strongly aggregated each other by intermolecular hydrogen bonds than those of MA-L-M, the rate of radical polymerization of MA-LA-M may be larger than that of MA-L-M. In this paper, syntheses and radical polymerization behavior of methacrylamides having peptide moieties, *N*-(methacryloylglycyl)-L-leucyl-L-alanine methyl ester (MA-GLA-M) and *N*-(methacryloyl-*β*-alanyl)-L-leucyl-L-alanine methyl ester (MA-*β*LA-M), are described. Furthermore, the differences in the structures of the polymers obtained from MA-LA-M, MA-GLA-M, and MA-*β*LA-M are discussed based on the measurement of CD and IR spectra.



Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM EX-90 and EX-400 spectrometers using tetramethylsilane (TMS) and hexamethyldisiloxane as internal standards in deuterochloroform ($CDCl_3$), deuteromethanol (CD_3OD), and deutero-*N*,*N*-dimethylformamide (DMF-d_7). FT-IR spectra were obtained with a Jasco FT/IR-5300. CD spectra were obtained by a Jasco J-720W spectropolarimeter in 2,2,2-trifluoroethanol (1.0 mmol/L, 0.10 cm cell). Melting points (mp) were measured by a Yanaco micro melting point apparatus. Molecular rotations ($[M]_D$) were measured on a Jasco DIP-1000 digital polarimeter using a sodium lamp as a light source. Molecular weights ($\overline{M}_n$) and distributions ($\overline{M}_w/\overline{M}_n$) were estimated by gel permeation chromatography (GPC) on a Tosoh HPLC HLC-8020 system with a data processor, equipped with four polystyrene gel columns (TSK gel G6000H, G5000H, G4000H, and G2500H), using DMF (5.8 mM lithium bromide solution) as an eluent at a flow rate of 1.0 mL/min, polystyrene calibration, and refractive index (RI) and ultraviolet (UV) detectors. Thermal analyses were performed on Seiko Instruments TG/DTA220. The 10% weight loss temperature (T_{d10}) was determined by thermogravimetric analysis (TGA) at a heating rate of 10 °C/min under a nitrogen atmosphere.

Materials. [1-Ethyl-3-(dimethylamino)prop-3-yl]carbodiimide hydrochloride (EDC•HCl) and di-*tert*-butyl dicarbonate (DiBoc) were offered from Eiweiss Chemical Co. 1-Hydroxybenzotriazole (HOBt), trifluoroacetic acid (TFA), 2,2,2-trifluoroethanol (TFE), methacrylic acid, and 2,2′-azobis(isobutyronitrile) (AIBN) were purchased from Tokyo Chemical Co.

* To whom all correspondence should be addressed.
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Ltd. *N*,*N*-Dimethylformamide (DMF) was distilled over calcium hydride. MeOH was distilled over magnesium methoxide.

Syntheses of Monomers. *N*-[(*tert*-Butoxycarbonyl)-glycyl]-L-leucyl-L-alanine Methyl Ester (Boc-GLA-M). To a solution of *N*-(*tert*-butoxycarbonyl)-L-leucyl-L-alanine methyl ester (Boc-LA-M; 5.0 g, 15.8 mmol)[5] in dichloromethane (50 mL) was added TFA (10 mL, 59.0 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated by rotary evaporation and dried in vacuo. To the solution of the residual compound in dichloromethane (50 mL) were added triethylamine (3.00 mL, 21.0 mmol), Boc-Gly-OH (3.05 g, 17.5 mmol), HOBt (2.66 g 17.5 mmol), and then EDC·HCl (3.33 g, 17.5 mmol) at 0 °C, and the resulting mixture was stirred at room temperature overnight. The reaction mixture was washed with water (50 mL), 0.5 M citric acid (50 mL), a saturated aqueous solution of $NaHCO_3$ (10 mL), and a saturated aqueous solution of NaCl (10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtrated, and concentrated by rotary evaporation. The residue was purified by recrystallization from ethyl acetate/ether (9/1, volume ratio): yield 3.78 g (75%); mp 183−184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (d, J = 6.40 Hz, 6 H, Leu$^\delta$), 1.40 (d, J = 6.80 Hz, 3 H, Ala$^\beta$), 1.46 (s, 9 H, (CH_3)$_3$C), 1.55−1.62 (m, 1 H, Leu$^\beta$), 1.65−1.70 (m, 2 H, Leu$^\gamma$), 3.75 (s, 3 H, CO_2CH_3), 3.83−3.85 (d, J = 5.60 Hz, 2 H, Gly$^\alpha$), 4.51−4.58 (m, 2 H, Leu$^\alpha$ and Ala$^\alpha$), 5.43 (broad, 1 H, Gly-NH), 6.90 (broad d, J = 7.20 Hz, 1 H, Ala-NH), 6.98 (broad d, J = 6.8 Hz, 1 H, Leu-NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.00 (Ala$^\beta$), 22.09 and 22.88 (Leu$^\delta$), 24.67 (Leu$^\gamma$), 28.31 ((CH_3)$_3$C−), 41.33 (CH_3)$_3C$−), 44.30 (Leu$^\beta$), 48.11 (Ala$^\alpha$), 51.61 (Leu$^\alpha$), 52.43 (CO_2CH_3), 156.09 (C═O (urethane)), 171.83 and 173.08 (C═O (amide)), 178.60 (C═O (ester)); IR (KBr) 3287 and 3075 (N−H), 2957 and 2872 (C−H), 1757 (C═O (ester)), 1636 (C═O (amide)), 1547 (N−H), 1458, 1385, 1280, 1205, 1167, 849 cm^{-1}.

***N*-(Methacryloylglycyl)-L-leucyl-L-alanine Methyl Ester (MA-GLA-M).** To a solution of Boc-GLA-M (3.0 g, 8.0 mmol) in dichloromethane (20 mL) was added TFA (5 mL, 29.6 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated by rotary evaporation and dried in vacuo. To the residual compound were added triethylamine (1.5 mL, 10.7 mmol), methacrylic acid (0.82 mL, 9.6 mmol), HOBt (1.47 g, 9.6 mmol), dichloromethane (30 mL), and then EDC·HCl (1.85 g, 9.6 mmol) at 0 °C, and the resulting mixture was stirred at room temperature overnight. The reaction mixture was washed with water (20 mL), 1 M HCl (20 mL), a saturated aqueous solution of $NaHCO_3$ (20 mL), and a saturated aqueous solution of NaCl (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtrated, and concentrated by rotary evaporation. The residue was purified by recrystallization from ethyl acetate/*n*-hexane (1/1, volume ratio): yield 1.55 g (57%); mp 157−158 °C; $[M]_D^{25}$ −126.0° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (d, J = 6.00 Hz, 3 H, Leu$^\delta$), 0.93 (d, J = 6.40 Hz, 3 H, Leu$^\delta$), 1.38 (d, J = 7.60 Hz, 3 H, Ala$^\beta$), 1.57 (m, 1 H, Leu$^\gamma$), 1.67 (m, 2 H, Leu$^\beta$), 1.97 (s, 3 H, CH_3 (allyl)), 3.73 (s, 3 H, CO_2CH_3), 4.06 (d, J = 5.20 Hz, 2 H, Gly$^\alpha$), 4.51−4.56 (m, 2 H, Leu$^\alpha$ and Ala$^\alpha$), 5.38 (s, 1 H, CH (olefin)), 5.79 (s, 1 H, CH (olefin)), 7.08−7.13 (broad, 2 H, Gly-NH, Leu-NH, and Ala-NH), 7.40 (broad d, J = 7.20 Hz, 1 H, Ala-NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.87 (Ala$^\beta$), 18.49 (CH_2═C(CH_3)), 22.02 and 22.81 (Leu$^\delta$), 24.69 (Leu$^\gamma$), 41.33 (Leu$^\beta$), 43.29 (Gly$^\alpha$), 48.12 (Ala$^\alpha$), 51.90 (Leu$^\alpha$), 52.40 (CO_2CH_3), 120.81 (CH_2═C), 139.01 (CH_2═*C*), 168.27, 169.29, and 171.93 (C═O (amide)), 173.13 (C═O (ester)); IR (KBr) 3295 (N−H), 2959 (C−H), 1755 (C═O (ester)), 1657 and 1651 (C═O (amide)), 1547 (N−H), 1208, 1169, 934 cm^{-1}. Anal. Calcd for $C_{16}H_{27}N_3O_5$: C, 56.29; H, 7.98; N, 12.31. Found: C, 56.23; H, 8.02; N, 12.29.

***N*[(-*tert*-Butoxycarbonyl)-*β*-alanyl]-L-leucyl-L-alanine Methyl Ester (Boc-*β*LA-M).** The title compound was prepared from Boc-LA-M and Boc-*β*-Ala-OH similarly to Boc-GLA-M. The purification was carried out by recrystallization from ethyl acetate/ether (1/5, volume ratio): yield 70%; mp 132−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, J = 5.60 Hz, 3 H, Leu$^\delta$), 0.94 (d, J = 5.60 Hz, 3 H, Leu$^\delta$), 1.39 (d, J = 6.80 Hz, 3 H, Ala$^\beta$), 1.43 (s, 9 H, (CH_3)$_3$C−), 1.49−1.59 (m, 1 H, Leu$^\gamma$), 1.62−1.71 (m, 2 H, Leu$^\beta$), 2.38−2.42 (m, 2 H, NHCH_2CH_2CO), 3.93 (m, 2 H, NHCH_2CH_2CO), 3.74 (s, 3 H, CO_2CH_3), 4.45−4.57 (m, 2 H, Leu$^\alpha$ and Ala$^\alpha$), 5.30 (broad, 1 H, N*H*CH_2CH_2CO), 6.79−6.95 (broad, 2 H, NH (amide)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.03 (Ala$^\beta$), 22.11 and 22.88 (Leu$^\delta$), 24.76 (Leu$^\gamma$), 28.42 ((CH_3)$_3$C−), 36.17 (NHCH_2*C*H_2CO), 38.78 (NH*C*H$_2$CH$_2$CO), 41.25 (Leu$^\beta$), 48.08 (Ala$^\alpha$), 51.72 (Leu$^\alpha$), 52.43 (CO_2CH_3), 156.07 (C═O (urethane)), 171.70 and 171.91 (C═O (amide)), 173.17 (C═O (ester)); IR (KBr) 3288 and 3073 (N−H), 2957 (C−H), 1746 (C═O (ester)), 1658 (C═O (amide)), 1543 (N−H), 1452, 1215, 1157, 985, 893 cm^{-1}.

***N*-(Methacryloyl-*β*-alanyl)-L-leucyl-L-alanine Methyl Ester (MA-*β*LA-M).** The title compound was prepared from Boc-*β*LA-M similarly to MA-GLA-M. The purification was carried out by recrystallization from ethyl acetate/*n*-hexane (1/9, volume ratio): yield 53%; mp 132−134 °C; $[M]_D^{25}$ −132.9° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, J = 6.40 Hz, 3 H, Leu$^\delta$), 0.93 (d, J = 7.20 Hz, 3 H, Leu$^\delta$), 1.39 (d, J = 7.20 Hz, 3 H, Ala$^\beta$), 1.54−1.65 (m, 3 H, Leu$^\beta$ and Leu$^\gamma$), 1.94 (s, 3 H, CH_3 (allyl)), 2.48−2.53 (m, 2 H, NHCH_2CH_2CO), 3.58 (m, 2 H, NHCH_2CH$_2$CO), 3.74 (s, 3 H, CO_2CH_3), 4.49−4.55 (m, 2 H, Leu$^\alpha$ and Ala$^\alpha$), 5.31 (s, 1 H, CH (olefin)), 5.71 (s, 1 H, CH (olefin)), 6.79−6.95 (broad, 3 H, NH (amide)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.97 (Ala$^\beta$), 18.46 (CH_2═C(CH_3)), 21.90 and 22.78 (Leu$^\delta$), 24.66 (Leu$^\gamma$), 35.38 (NHCH_2*C*H$_2$CO), 35.78 (NHCH_2CH$_2$CO), 41.16 (Leu$^\beta$), 47.98 (Ala$^\alpha$), 51.73 (Leu$^\alpha$), 52.35 (CO_2CH_3), 119.72 (CH_2═C), 139.66 (CH_2═*C*), 168.41, 171.77, and 171.86 (C═O (amide)), 173.09 (C═O (ester)); IR (KBr) 3288 and 3073 (N−H), 2957 (C−H), 1746 (C═O (ester)), 1658 (C═O (amide)), 1635 (C═C), 1543 (N−H), 1452, 1215, 1157, 985, 893 cm^{-1}. Anal. Calcd for $C_{17}H_{29}N_3O_5$: C, 57.45; H, 8.22; N, 11.82. Found: C, 57.81; H, 8.21; N, 11.82.

Radical Polymerization. To MA-GLA-M (341 mg, 1.0 mmol) or MA-*β*LA-M (355 mg, 1.0 mmol) in a polymerization tube were introduced AIBN (1.64 mg, 1 mol %) and DMF or MeOH (1.0 mL). The tube was cooled, degassed, sealed off, and heated at 60 °C for 20 h. The resulting mixture was diluted with methanol (10 mL) and precipitated with ether (300 mL). The solvent-insoluble part was filtered off and dried at 50 °C overnight in vacuo.

Measurements of Time−Conversion of Monomers. Time−conversions of radical polymerization of MA-LA-M, MA-GLA-M, and MA-*β*LA-M with AIBN (1 mol %) in CD_3OD and DMF-d_7 (1.0 mol/L) in degassed sealed NMR sample tubes were monitored by ^{1}H NMR (400 MHz) spectra following the decrease of signals of olefin protons toward the internal standard (hexamethyldisiloxane) at 60 °C, respectively. The ^{1}H NMR spectra were measured first at room temperature. After that, the sample tube was ejected from the NMR probe, and the probe was heated to the set temperature. The time−conversion measurement was started by inserting the sample tube into the probe. The conversions of the monomers were estimated based on ^{1}H NMR spectra measured at room temperature. The rate constants of polymerization were reproduced within ±3%.

Results and Discussion

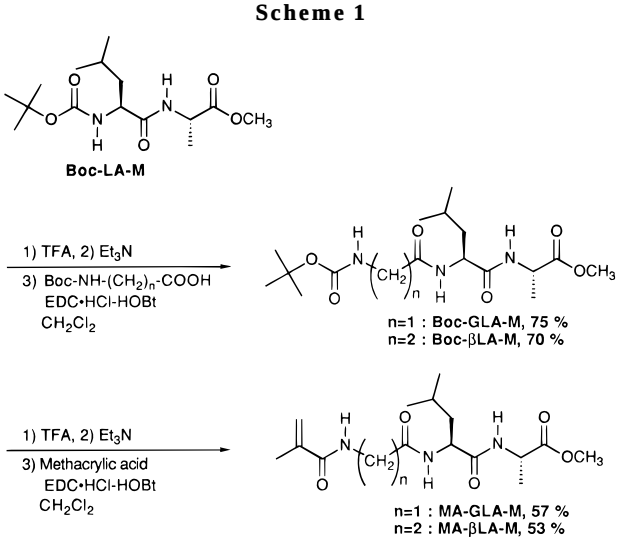
Syntheses of Monomers. The monomers, MA-GLA-M and MA-*β*LA-M, were prepared by the condensation reactions of glycyl-L-leucyl-L-alanine methyl ester trifluoroacetate (TFA·Gly-Leu-Ala-OMe) and *β*-alanyl-L-leucyl-L-alanine methyl ester trifluoroacetate (TFA·*β*-Ala-Leu-Ala-OMe) with methacrylic acid using EDC·HCl and HOBt as coupling reagents in the presence of triethylamine, as shown Scheme 1. TFA·Gly-Leu-Ala-OMe and TFA·*β*-Ala-Leu-Ala-OMe were prepared by the coupling reactions of L-leucyl-L-alanine methyl ester trifluoroacetate (TFA·Leu-Ala-OMe) and *N*-(*tert*-butoxycarbonyl)glycine (Boc-Gly-OH) or -*β*-alanine (Boc-*β*-Ala-OH) using the EDC·HCl-HOBt method, followed by deprotection of the Boc group by TFA. The structures of the monomers were confirmed by ^{1}H and ^{13}C NMR and IR spectra besides elemental analyses. TFA·Leu-

Table 1. Radical Polymerizations of Monomers Having Dipeptide Moieties[a]

run	monomer	solvent	conversion[b] (%)	yield[c] (%)	$\bar{M}_n$[d]	$\bar{M}_w/\bar{M}_n$[d]	Td_{10}[e] (°C)	$[M]_D$[f] (deg)
1	MA-GLA-M	DMF	97	92	68 000	2.54	288	-176.5
2	MA-GLA-M	MeOH	98	79	136 000	2.07	287	-156.7
3	MA-βLA-M	DMF	95	93	69 000	2.27	295	-242.1
4	MA-βLA-M	MeOH	88	77	77 000	1.69	295	-225.0
5	MA-LA-M[g]	DMF	98	90	75 000	2.22	311	-217.5
6	MA-LA-M	MeOH	69	62	41 000	1.93	311	-211.0

[a] Conditions: monomer, 1 mmol; initiator, 2,2′-azobis(isobutyronitrile) (AIBN), 1 mol %; concentration, 1.0 mol/L; 60 °C; 20 h. [b] Estimated by ^{1}H NMR. [c] Ether-insoluble part. [d] Estimated by GPC based on polystyrene standards; eluent, LiBr solution in DMF (5.8 mM). [e] Determined by TGA under nitrogen. [f] Measured by a polarimeter at 25 °C (*c* 1.00, $CHCl_3$). [g] Ref 5.

Scheme 1



Ala-OMe was prepared according to the method reported previously.[5]

Radical Polymerizations of MA-GLA-M and MA-βLA-M. Radical polymerizations of MA-GLA-M and MA-βLA-M were carried out at 60 °C for 20 h in DMF (1.0 mol/L) in the presence of AIBN (1 mol %). The obtained polymer was isolated by reprecipitation with ether. The conversions of the monomers estimated by the ^{1}H NMR were nearly quantitative, and the obtained polymers were confirmed as poly(MA-GLA-M) and poly(MA-βLA-M) by their ^{1}H NMR spectra (Figures 1 and 2). The conditions and results of their polymerizations are summarized in Table 1 (runs 1 and 3). In the radical polymerizations of MA-GLA-M and MA-βLA-M, large increases of absolute values of specific rotations in the transformation from the monomers (−126.0°, MA-GLA-M; −132.9°, MA-βLA-M) to polymers (−176.5 and −242.1 °, respectively) were observed similarly to the polymerization of MA-LA-M.[5] On the other hand, radical polymerization of the monomers was carried out in MeOH (1.0 mol/L) with the similar method mentioned above. The conversions of polymerizations of MA-GLA-M and MA-βLA-M (98 and 88%, respectively, runs 2 and 4) were larger than that of MA-LA-M (69%). The molecular weight of poly(MA-GLA-M) ($\bar{M}_n$ = 136 000) was larger than those of MA-βLA-M and MA-LA-M (77 000 and 41 000, respectively).

The time−conversion relationships of the monomers at 60 °C in DMF-d_7 (Figure 3) and in CD_3OD (Figure 4) were compared. No significant difference was observed between the polymerizations of the three monomers in DMF-d_7 as shown in Figure 3. Meanwhile, the polymerization rate of MA-GLA-M in CD_3OD was apparently larger than those of MA-βLA-M and MA-LA-M as shown Figure 4. The polymerization rate constants (k) of the monomers were estimated according to the following

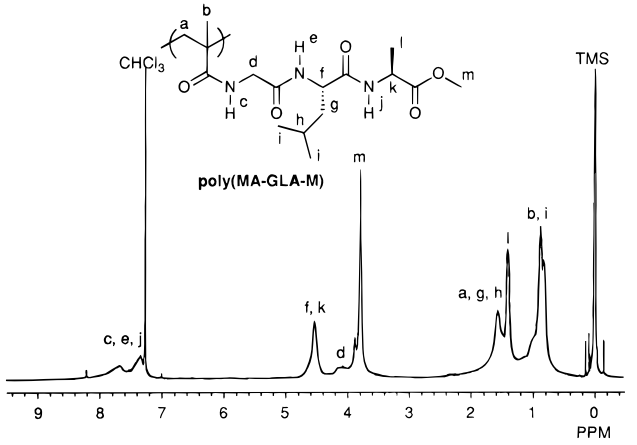


Figure 1. ^{1}H NMR spectrum (400 MHz) of poly(MA-GLA-M) (run 1 in Table 1, solvent $CDCl_3$ containing trifluoroacetic acid (1 vol %)).

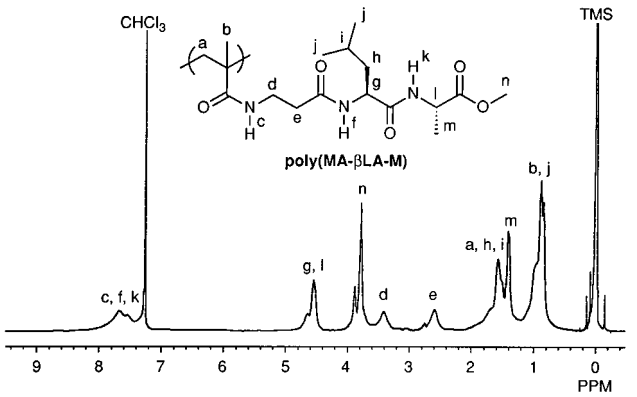


Figure 2. ^{1}H NMR spectrum (400 MHz) of poly(MA-βLA-M) (run 3 in Table 1, solvent $CDCl_3$ containing trifluoroacetic acid (1 vol %)).

equation (1). The exponents of the monomer concentration (m) and initiator concentration (n) may be assumed to be 1 and 0.5, respectively.

$$k = R_p/[M]^m[I]^n \quad (1)$$

The results obtained are summarized in Table 2, which show that the polymerization rate of MA-GLA-M is 2 times larger than that of MA-βLA-M and 6 times larger than that of MA-LA-M in CD_3OD. On the other hand, the polymerization rates in DMF-d_7 of the three monomers showed only small differences.

In the IR spectra of MA-GLA-M, MA-βLA-M, and MA-LA-M in MeOH (1.0 mol/L) at room temperature, MA-GLA-M showed IR absorption peaks at 1632 (amide I region) and 1554 cm^{-1} (amide II region). MA-βLA-M showed absorption peaks at 1641 and 1541 cm^{-1}, and MA-LA-M showed them at 1660 and 1535 cm^{-1}. These results suggest that the aggregation of the monomers

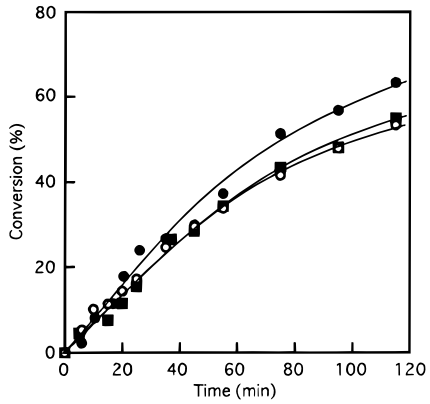


Figure 3. Time−conversion relationships in the radical polymerizations of MA-GLA-M, MA-βLA-M, and MA-LA-M initiated by AIBN in DMF-d_7 at 60 °C: [M] = 1.0 mol/L; [AIBN] = 0.010 mol/L. (●) MA-GLA-M, (○) MA-βLA-M, (■) MA-LA-M.

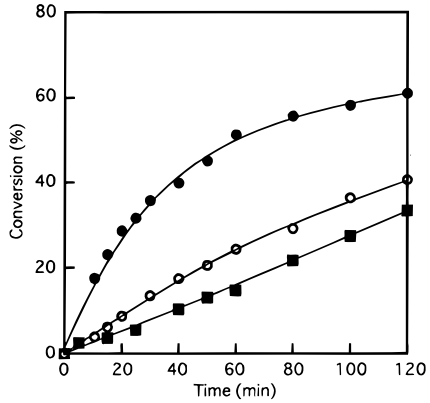
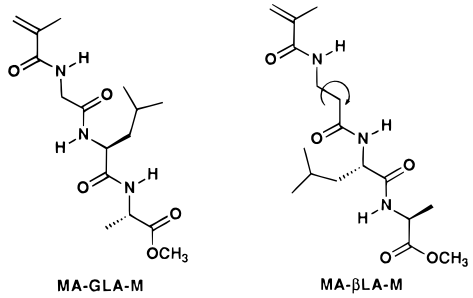


Figure 4. Time−conversion relationships in the radical polymerizations of MA-GLA-M, MA-βLA-M, and MA-LA-M initiated by AIBN in CD_3OD at 60 °C: [M] = 1.0 mol/L; [AIBN] = 0.010 mol/L. (●) MA-GLA-M, (○) MA-βLA-M, (■) MA-LA-M.

Table 2. Polymerization Rate Constants (k) of Monomers Having Dipeptide Moieties[a]

	k at 60 °C ($L^{1/2}\cdot mol^{-1/2}\cdot s^{-1}$)	
monomer	in DMF-d_7	in CD_3OD
MA-GLA-M	14.5×10^{-4}	18.1×10^{-4}
MA-βLA-M	12.2×10^{-4}	7.83×10^{-4}
MA-LA-M	12.7×10^{-4}	3.76×10^{-4}

Chart 1



by hydrogen bonding was the following order: MA-GLA-M > MA-βLA-M > MA-LA-M. We reported that the radical polymerizability would be influenced by the aggregation of the monomers by intermolecular hydrogen bonds.[5] MA-GLA-M and MA-βLA-M have one more unit capable of hydrogen bonding than MA-LA-M; therefore, MA-GLA-M and MA-βLA-M might be more aggregated by hydrogen bonding to show larger polymerizability than MA-LA-M. The larger polymerizability

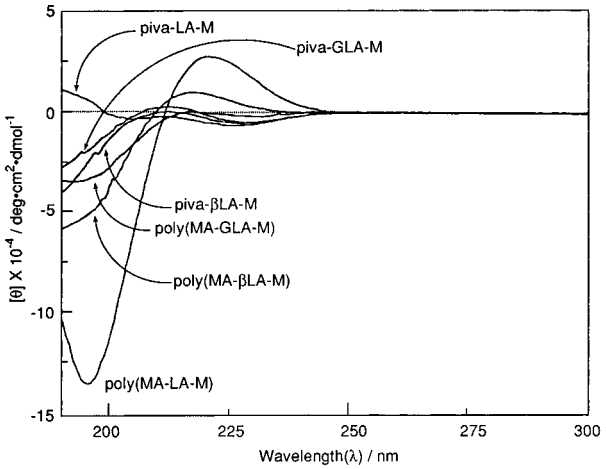


Figure 5. CD spectra of poly(MA-LA-M), poly(MA-GLA-M), poly(MA-βLA-M), piva-LA-M, piva-GLA-M, and piva-βLA-M measured in 2,2,2-trifluoroethanol (1.0 mmol/L).

of MA-GLA-M in MeOH than that of MA-βLA-M might be caused by the more rigid structure of the former than that of the latter as illustrated in Chart 1. On the other hand, the IR absorption peaks of the amide I and II reagions of MA-GLA-M were observed at 1664 and 1541 cm^{-1} in DMSO (1.0 mol/L), which were very close to those of MA-βLA-M (1666 and 1547 cm^{-1}) and MA-LA-M (1662 and 1531 cm^{-1}).[6] These results suggest that the degrees of aggregation of these monomers in DMSO have no significant difference, probably in DMF, neither. Consequently, the radical polymerization rates of the three monomers would be equal in DMF.

The effect of methylene chains on the structures of the polymers obtained was investigated. The CD spectra for the polymers and model compounds are shown in Figure 5. Strong positive and negative peaks were observed at 223 and 197 nm, respectively, in the CD spectrum of poly(MA-LA-M). The former is attributable to the n−π^* transition and the latter to the $\pi-\pi^*$ transition of the amide group.[7] The CD pattern for poly(MA-LA-M) was rather different from that of the model compound (piva-LA-M), as shown in Figure 3. On the other hand, the CD patterns of poly(MA-GLA-M) and poly(MA-βLA-M) were similar to those of the corresponding model compounds and showed no strong peaks at 180−250 nm. These results may suggest that poly(MA-GLA-M) and poly(MA-βLA-M), which have methylene chains between the methacrylamide and LA peptide moieties, form no special conformation differently from poly(MA-LA-M). The special conformation of poly(MA-LA-M) might be caused by the interaction between the propagating polymer end and the optically active bulky peptide side chain of the monomers.[8]

FT-IR spectroscopic studies of the polymers in chloroform (0.05 mol/L) were performed, as shown in Figure 6. Poly(MA-GLA-M) and poly(MA-βLA-M) showed single absorption peaks at 1655 and 1643 cm^{-1} in the amide I region, respectively. The all-carbonyl groups of the amide moieties of the two polymers are suggested to participate in hydrogen bonding. On the other hand, poly(MA-LA-M) showed two absorption peaks at 1678 and 1642 cm^{-1} in that region, which could be assigned as non-hydrogen-bonding and hydrogen-bonding carbonyl groups, respectively. The distance from the polymer main chain to the bulky LA peptide moiety is in the order poly(MA-βLA-M) > poly(MA-GLA-M) > poly(MA-LA-M), which well agrees with that of the strength of hydrogen bonding of the polymer systems. No IR shift

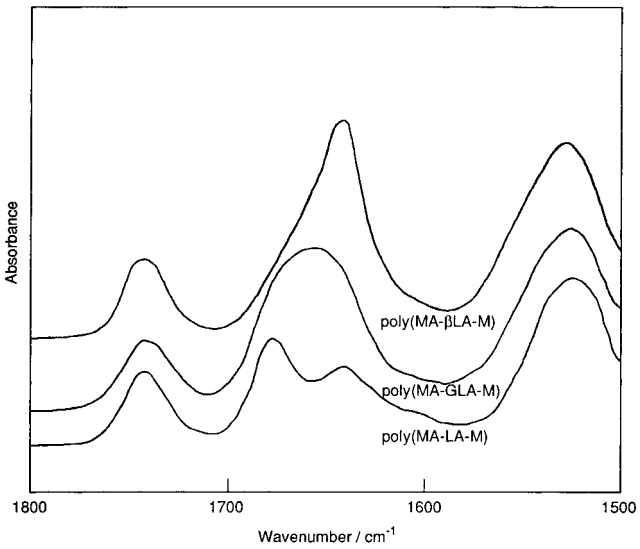


Figure 6. IR spectra of poly(MA-LA-M), poly(MA-GLA-M), and poly(MA-βLA-M) measured in $CHCl_3$ (0.05 mol/L).

of the carbonyl absorption peak was observed by the addition of TFE or DMSO (5−20 vol %) to the former two polymer solutions in $CHCl_3$. This indicates that the peptide moieties in the polymer side chains strongly aggregated each other by intramolecular hydrogen bonding.

Summary

In this paper, the syntheses and radical polymerization behavior of methacrylamides having peptide moieties, *N*-(methacryloylglycyl)-L-leucyl-L-alanine methyl ester (MA-GLA-M) and *N*-(methacryloyl-β-alanyl)-L-leucyl-L-alanine methyl ester (MA-βLA-M), were studied, and their polymerizabilities were compared with that of *N*-methacryloyl-L-leucyl-L-alanine methyl ester (MA-LA-M). MA-GLA-M and MA-βLA-M were prepared by the condensations of methacrylic acid with glycyl-L-leucyl-L-alanine and β-alanyl-L-leucyl-L-alanine methyl ester trifluoroacetates using the EDC·HCl-HOBt method, respectively. These monomers underwent radical polymerizations satisfactorily to afford the corresponding polymers. The rates of the radical polymerizations of the three monomers in MeOH were in the order MA-GLA-M > MA-βLA-M > MA-LA-M, which would reflect the degree of aggregation between the monomers. The CD patterns of poly(MA-GLA-M) and poly(MA-βLA-M) were similar to those of the corresponding model compounds, pivaloylamides. The all amide carbonyl groups of the polymers are suggested to participate in hydrogen bonding from the IR analyses. The amide carbonyl absorption of poly(MA-βLA-M) was observed at 1643 cm^{-1}, which shifted to 12 cm^{-1} lower than that of poly(MA-GLA-M), probably due to the larger flexibility of the LA moiety of the former.

Supporting Information Available: Experimental details of the syntheses of Boc-Gly-OH, Boc-β-Ala-OH, and model compounds (piva-LA-M, piva-GLA-M, and piva-βLA-M) and Figure SI, a CD spectrum of poly(MA-L-M) measured in TFE (1.0 mmol/L) (4 pages). Ordering information is given on any current masthead page.

References and Notes

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(8) The similar CD patterns of poly(MA-LA-M) and poly(MA-L-M) indicate the special conformation of the two polymers is derived to the same principle (see supporting information, Figure SI). The larger isotacticity of poly(MA-L-M) (syndio:hetero:iso = 46:41:13) than that of poly(MMA) (syndio:hetero:iso = 59:36:5) prepared in a similar radical condition may be concerned with the special conformation.

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