

# Syntheses of functionalized polymethacrylamides based on methionine oxides

Fumio Sanda, Futoshi Ogawa and Takeshi Endo\*

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

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Radical polymerizations of methacrylamides having methionine, methionine sulfoxide, and methionine sulfone moieties, and oxidations of the polymethacrylamide having a methionine moiety were examined. The radical polymerizations of the monomers were carried out using 2,2'-azobis(isobutyronitrile) (AIBN) as an initiator to afford the corresponding polymers in good yields. The polymer with a methionine structure was oxidized by 2 and 10 equivalents of hydrogen peroxide to obtain polymers having methionine sulfoxide and sulfone structures in the side chains, respectively. © 1998 Elsevier Science Ltd. All rights reserved.

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## INTRODUCTION

Syntheses, structures, and properties of synthetic peptides have been examined as models of proteins (For examples see Refs 1–4. Amino acids, components of peptides, are widely used for drugs and foods. Recent remarkable advances on fermentation and chemical synthetic methods have enabled us to obtain amino acids with high optical purity and lower price. Consequently, various vinyl polymers having amino acid moieties in the side chains have been developed<sup>5–24</sup>. Unique polymerization behaviour, structure, and properties of the polymers are expected based on the chirality. Meanwhile, polymethionine shows high biocompatibility and is expected to be used as medical materials such as contact lenses<sup>25</sup>, artificial skins<sup>26</sup>, internal organs<sup>27</sup> and blood vessels<sup>28</sup>. Polymethionine membrane shows high oxygen permeability and its oxidized membrane shows higher oxygen permeability<sup>29–31</sup>. Therefore, synthesis of a vinyl polymer having a methionine moiety in the side chain will be useful for development of novel biocompatible functional polymers. In this paper, syntheses and radical polymerizations of methacrylamides having methionine, methionine sulfoxide, and methionine sulfone structures, and oxidation of the polymer are disclosed.

## EXPERIMENTAL

### Measurements

<sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance (n.m.r.) spectra were recorded on a JEOL JNM EX-90 and an EX-400 spectrometers using tetramethylsilane (TMS) as an internal standard in chloroform-*d* (CDCl<sub>3</sub>) or *N,N*-dimethylformamide (DMF-*d*<sub>7</sub>). Infra-red (i.r.) spectra were obtained with a JASCO FT/IR-5300. Melting points (mp) were measured by a Yanaco micro melting point apparatus. Specific rotations ([α]<sub>D</sub>) were measured on a JASCO DIP-1000 digital

polarimeter using a sodium lamp as a light source. Molecular weights ( $\bar{M}_n$ ) and the distributions ( $\bar{M}_w/\bar{M}_n$ ) were estimated by gel permeation chromatography (g.p.c.) on a Tosoh HPLC HLC-8020 system with a data processor, equipped with four polystyrene gel columns (TSK gels, 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<sup>-1</sup>, polystyrene calibration, and refractive index and ultra-violet (u.v.) detectors. Thermal analyses were performed on a Seiko Instruments TG/DTA220 and DSC220C. The glass transition temperature ( $T_g$ ) was taken by differential scanning calorimetry (d.s.c.) as an inflection point on a trace at a heating rate of 10°C min<sup>-1</sup>. The 10% weight loss temperature ( $T_{d10}$ ) was determined by thermogravimetric analysis (t.g.a.) at a heating rate of 10°C min<sup>-1</sup> under a nitrogen atmosphere. Refractive indexes were measured by an Atago Abbe's refractometer.

### Materials

(L)- and (D)-methionines (Nihon Soda), 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC·HCl, Eiwiss Chemical Co.), 2,2'-azobis(isobutyronitrile) (AIBN, Tokyo Chemical Industry Co.) were used as received. Chlorobenzene was distilled over calcium hydride after washing with concentrated sulfuric acid, aqueous sodium hydrogen carbonate, and water. DMF was distilled over calcium hydride.

### Syntheses of monomers

*N*-methacryloyl-(L)-methionine methyl ester (MA-(L)-M-M), *N*-methacryloyl-(D)-methionine methyl ester (MA-(D)-M-M), and *N*-methacryloyl-(D,L)-methionine methyl ester (MA-(D,L)-M-M). The title compounds were synthesized from the corresponding methionines according to the reported method<sup>24</sup>.

*MA-(L)-M<sub>SO</sub>-M*. To a solution of MA-(L)-M-M (5.55 g, 24 mmol) in methanol (50 ml) was added an aqueous

\* To whom correspondence should be addressed

solution of sodium metaperiodate (0.5 M, 50.4 mL, 28.8 mmol) at 0°C. After stirring for 6 h, a precipitate formed was filtered off, and the filtrate was extracted by chloroform. The organic layer was dried over anhydrous magnesium sulfate and concentrated by rotary evaporation. The residue was purified by silica gel column chromatography eluted by methanol to afford a pale yellow liquid. Yield 5.18 g (87%), <sup>1</sup>H n.m.r. (90 MHz, CDCl<sub>3</sub>) δ 6.66–7.23 (1H, m, –NH), 5.76 (1H, s, CH<sub>2</sub>=C(CH<sub>3</sub>)–), 5.43 (1H, s, CH<sub>2</sub>=C(CH<sub>3</sub>)–), 4.72–4.84 (1H, m, >CHCO<sub>2</sub>CH<sub>3</sub>), 3.76 (3H, s, –CO<sub>2</sub>CH<sub>3</sub>), 2.75–2.93 (2H, m, –CH<sub>2</sub>SO–), 2.59 (3H, s, CH<sub>3</sub>SO–), 2.20–2.55 (2H, m, –CH<sub>2</sub>CH<sub>2</sub>SO–), 1.96 (3H, s, CH<sub>2</sub>=C(CH<sub>3</sub>)–), <sup>13</sup>C n.m.r. (100 MHz, CDCl<sub>3</sub>) δ 171.9 (–CONH–), 168.5 (–CO<sub>2</sub>–), 139.1 (CH<sub>2</sub>=C(CH<sub>3</sub>)–), 120.8 (CH<sub>2</sub>=C(CH<sub>3</sub>)–), 52.7, 51.3, 50.1, 38.4, 25.5, 18.5, i.r. (neat) 1744 (νCOOMe), 1660 (νCONH), 1624 (νC=C), 1530 (νNH), 1439, 1307, 1205, 1026 (νS=O), 930 cm<sup>-1</sup>. EA. Calcd for C<sub>10</sub>H<sub>17</sub>NO<sub>4</sub>S, C, 48.57; H, 6.93; N, 5.66; S, 12.96. Found: C, 48.61; H, 7.16; N, 5.96; S, 12.56.

*MA-(L)-M<sub>SO<sub>2</sub>-M</sub>*. To a solution of MA-(L)-M-M (2.98 g, 12.9 mmol) of chloroform (13 mL) was added an aqueous hydrogen peroxide solution (35%, 12.5 mL, 129 mmol) at 0°C, and stirred at 0°C overnight. Organic compounds were extracted from the reaction mixture by ethyl acetate, and the extract was purified by silica gel column chromatography eluted by ethyl acetate to afford a pale yellow liquid. Yield 1.30 g (42%). <sup>1</sup>H n.m.r. (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.24–8.39 (1H, m, –NH), 5.78 (1H, s, CH<sub>2</sub>=C(CH<sub>3</sub>)–), 5.38 (1H, s, CH<sub>2</sub>=C(CH<sub>3</sub>)–), 4.42–4.50 (1H, m, >CHCO<sub>2</sub>CH<sub>3</sub>), 3.68 (3H, s, –CO<sub>2</sub>CH<sub>3</sub>), 3.10–3.18 (2H, m, –CH<sub>2</sub>SO<sub>2</sub>–), 2.98 (3H, s, –SO<sub>2</sub>CH<sub>3</sub>), 2.03–2.20 (2H, m, –CH<sub>2</sub>CH<sub>2</sub>SO<sub>2</sub>–), 1.86 (3H, m, CH<sub>2</sub>=C(CH<sub>3</sub>)–), i.r. (neat) 1741 (νCOOMe), 1658 (νCONH), 1618 (νC=C), 1531 (νNH), 1440, 1296, (νO=S=O), 1211, 1132 (νO=S=O), 1007. EA. Calcd for C<sub>10</sub>H<sub>17</sub>NO<sub>5</sub>S, C, 45.62; H, 6.51; N, 5.32; S, 12.18. Found: C, 45.47; H, 6.90; N, 5.19; S, 12.43.

*Pivaloyl-(L)-methionine methyl ester*. The title compound was prepared from (L)-methionine methyl ester hydrochloride and pivaloyl chloride similar to MA-(L)-M-M. Yield 95%, [α]<sub>D</sub><sup>25</sup> = +38.8° (c 1.00, CHCl<sub>3</sub>), <sup>1</sup>H n.m.r. (400 MHz, CDCl<sub>3</sub>) δ 6.42 (1H, broad s, –NH–), 4.67–4.72 (1H, m, >CHCO<sub>2</sub>CH<sub>3</sub>), 3.76 (3H, s, –CO<sub>2</sub>CH<sub>3</sub>), 2.49–2.53 (m, 2H, –CH<sub>2</sub>S–), 1.98–2.21 (m, 2H, –CH<sub>2</sub>CH<sub>2</sub>S–), 2.10 (s, 3H, –SCH<sub>3</sub>), 1.23 (9H, s, –C(CH<sub>3</sub>)<sub>3</sub>), <sup>13</sup>C n.m.r. (100 MHz, CDCl<sub>3</sub>) δ 178.3, 172.7, 52.4, 51.5, 38.7, 31.4, 30.0, 27.4, 15.5 ppm, i.r. (neat) 2963, 1743 (νCOOMe), 1649 (νCONH), 1524, 1202 cm<sup>-1</sup>. EA. Calcd for C<sub>11</sub>H<sub>21</sub>NO<sub>3</sub>S, C, 53.41; H, 8.56; N, 5.66; S, 12.96. Found: C, 53.42; H, 8.55; N, 5.28; S, 12.20.

#### Radical polymerization. General procedure

To a monomer (3 mmol) in a polymerization tube was introduced AIBN, and subsequently a dry solvent, if required. The tube was cooled, degassed, sealed off, and heated at 60°C for 20 h. The resulting mixture was diluted with chloroform (3 mL) and poured into ether (100 mL) to precipitate a polymer. The solvent-insoluble polymer was filtrated and dried at 50°C *in vacuo* overnight.

*Poly(MA-M-M)*. <sup>1</sup>H n.m.r. δ (CDCl<sub>3</sub>) 8.1–7.4 (m, 1H), 4.8–4.3 (m, 1H), 4.0–3.5 (m, 3H), 2.9–0.7 (m, 12H).

*Poly(MA-(L)-M<sub>SO</sub>-M)*. <sup>1</sup>H n.m.r. (400 MHz, DMF-*d*<sub>7</sub>) δ

7.46–8.02 (1H, broad s, –NH), 4.42–4.58 (1H, broad s, NHCHCO), 3.80 (3H, broad s, –CO<sub>2</sub>CH<sub>3</sub>), 3.02–3.06 (2H, m, –CH<sub>2</sub>SO–), 2.70 (3H, s, –SOCH<sub>3</sub>), 2.58–2.81 (2H, m, –CH<sub>2</sub>CH<sub>2</sub>SO–), 1.02–2.15 (5H, m), <sup>13</sup>C n.m.r. (100 MHz, DMF-*d*<sub>7</sub>) 179.2, 172.8, 52.6, 52.1, 51.5, 46.7, 40.3, 24.0, 17.9, i.r. (KBr) 1736 (νCOOMe), 1649 (νCONH), 1525, 1445, 1375, 1202, 1016 (νS=O) cm<sup>-1</sup>. EA. Calcd for C<sub>10</sub>H<sub>17</sub>NO<sub>4</sub>S, C, 48.57; H, 6.93; N, 5.66; S, 12.96. Found: C, 48.47; H, 7.02; N, 5.45; S, 12.75.

*Poly(MA-(L)-M<sub>SO<sub>2</sub>-M)</sub>*. <sup>1</sup>H n.m.r. (400 MHz, DMF-*d*<sub>7</sub>) δ 7.82–7.96 (1H, broad s, –NH), 4.42–4.68 (1H, broad s, NHCHCO), 3.80 (3H, broad s, –CO<sub>2</sub>CH<sub>3</sub>), 3.33–3.48 (2H, m, –CH<sub>2</sub>SO<sub>2</sub>–), 3.19 (3H, s, –SO<sub>2</sub>CH<sub>3</sub>), 1.02–2.53 (5H, m), <sup>13</sup>C n.m.r. (100 MHz, DMF-*d*<sub>7</sub>) δ 176.8, 172.3, 52.6, 18.6, i.r. (KBr) 1650 (νCONH), 1523, 1296, (νO=S=O), 1128 (νO=S=O), 966, 771 cm<sup>-1</sup>. EA. Calcd for C<sub>10</sub>H<sub>17</sub>NO<sub>5</sub>S, C, 45.62; H, 6.51; N, 5.32; S, 12.18. Found: C, 45.26; H, 6.00; N, 5.51; S, 12.26.

*Oxidation of poly(MA-(L)-M-M)*. To a solution of poly(MA-(L)-M-M) (2.31 g, 10 mmol for the monomer unit) in chloroform (10 mL) were added an aqueous hydrogen peroxide solution and water (30 mL), and the reaction mixture was vigorously stirred at room temperature for 24 h. The reaction mixture was concentrated by rotary evaporation to give an oxidized polymer.

*Pivaloyl-(L)-methionine sulfone methyl ester*. The title compound was prepared by the oxidation of pivaloyl-(L)-methionine methyl ester with two equivalents of hydrogen peroxide similar to the oxidation of poly(MA-(L)-M-M), and purified by preparative HPLC (Nihon Bunseki Kogyo), equipped with two polystyrene gel columns (JAIGELs H1 and H2), using chloroform as the eluent (flow rate 3.8 mL min<sup>-1</sup>, RI and u.v. detectors). Yield 95%, mp 74.5–76.0°C, [α]<sub>D</sub><sup>28</sup> = 28.7° (c 1.00, CHCl<sub>3</sub>), <sup>1</sup>H n.m.r. (400 MHz, CDCl<sub>3</sub>) δ 6.72 (1H, d, *J* = 7.6 Hz, –NH–), 4.62–4.68 (1H, m, >CHCO<sub>2</sub>CH<sub>3</sub>), 3.77 (3H, s, –CO<sub>2</sub>CH<sub>3</sub>), 3.15–3.22 (m, 1H, –CH<sub>2</sub>SO<sub>2</sub>–) 3.03–3.11 (m, 1H, –CH<sub>2</sub>SO<sub>2</sub>–), 2.96 (s, 3H, CH<sub>3</sub>SO<sub>2</sub>–), 2.38–2.46 (m, 1H, –CH<sub>2</sub>CH<sub>2</sub>SO<sub>2</sub>–), 2.18–2.26 (m, 1H, –CH<sub>2</sub>CH<sub>2</sub>SO<sub>2</sub>–), 1.22 (9H, s, (CH<sub>3</sub>)<sub>3</sub>C–), <sup>13</sup>C n.m.r. (100 MHz, CDCl<sub>3</sub>) δ 179.0, 171.7, 52.7, 51.1, 50.7, 40.6, 38.7, 27.6, 27.5, 27.3, 27.1, 25.0 ppm, i.r. (neat) 3355, 2967, 1738, 1644, 1526, 1304, 1246, 1128, 663 cm<sup>-1</sup>. EA. Calcd for C<sub>11</sub>H<sub>21</sub>NO<sub>5</sub>S, C, 47.30; H, 7.58; N, 5.01; S, 11.48. Found: C, 47.08; H, 7.39; N, 4.95; S, 11.21.

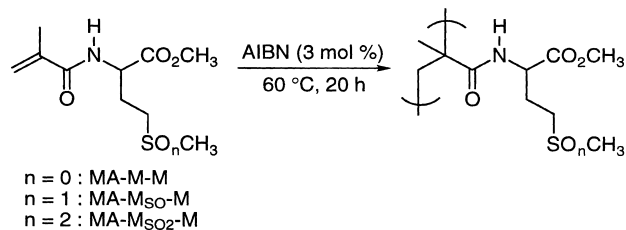
## RESULTS AND DISCUSSION

### Syntheses of the monomers

The monomers, *N*-methacryloyl-(L)-, -(D)-, and -(L,D)-methionine methyl esters [MA-(L)-M-M, MA-(D)-M-M, MA-(L,D)-M-M], were prepared from the corresponding methionine methyl ester hydrochlorides and methacrylic acid according to the previously reported method<sup>24</sup>. The methionine sulfoxide monomer [MA-(L)-M<sub>SO</sub>-M] and the sulfone monomer [MA-(L)-M<sub>SO<sub>2</sub>-M] were prepared by the oxidations of MA-(L)-M-M with sodium metaperiodate and hydrogen peroxide, respectively. The structures of the monomers were determined by <sup>1</sup>H and <sup>13</sup>C n.m.r. and i.r. spectra, besides elemental analyses.</sub>

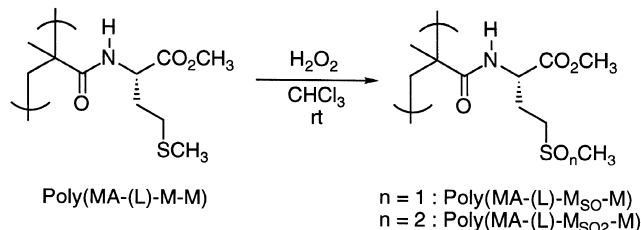
### Radical polymerizations

Radical polymerizations of the monomers were carried



Scheme 1

out in the presence of AIBN (1 mol%) at 60°C for 20 h in bulk, DMF, and chlorobenzene to isolate the polymers by precipitation with ether (Scheme 1). The structures of the polymers were determined as the corresponding polymethacrylamides by <sup>1</sup>H n.m.r. spectroscopy. The results and conditions of the polymerizations are summarized in Table 1. The lower conversion of MA-(L)-M-M in the bulk polymerization (run 1) than those in the solution polymerizations (runs 2 and 3) should be caused by the solidification of the polymerization mixture soon after the polymerization initiated, while the  $\bar{M}_n$  of the former polymer was much higher than those of the latter two polymers. No significant differences were observed in the  $[\alpha]_D^{25}$ ,  $T_g$ s, and  $T_{d10}$ s of the



Scheme 2

polymers obtained in the different conditions. The  $T_g$  of poly(MA-M<sub>SO<sub>2</sub></sub>-M) was higher than those of poly(MA-M<sub>SO</sub>-M) and poly(MA-M-M). The absolute value of the  $[\alpha]_D$  was in the following order; poly(MA-M<sub>SO</sub>-M) > poly(MA-M<sub>SO<sub>2</sub></sub>-M) > poly(MA-M-M).

#### Oxidation of poly(MA-(L)-M-M)

Hydrogen peroxide has been used as a common oxidant for sulfides to sulfoxides and sulfones. Poly(MA-(L)-M) was oxidized by several amounts of hydrogen peroxide as shown in Scheme 2 and Table 2. The ratio of the sulfide, sulfoxide, and sulfone units could be determined by the <sup>1</sup>H n.m.r. spectral integration ratio of the  $\alpha$ -methylene protons of the

**Table 1** Radical polymerizations of MA-(L)-M-M, MA-(D)-M-M, MA-(L,D)-M-M, MA-(L)-M<sub>SO</sub>-M, and MA-(L)-M<sub>SO<sub>2</sub></sub>-M

Run	Monomer	Solvent	Conv <sup>b</sup> (%)	Yield <sup>c</sup> (%)	$\bar{M}_n$ <sup>d</sup>	$\bar{M}_w/\bar{M}_n$ <sup>d</sup>	$[\alpha]_D^{25}$ (°)	$T_g^e$ (°C)	$T_{d10}^f$ (°C)
1	MA-(L)-M-M	None	76	64	509 000	2.64	+11.5	114	273
2	MA-(L)-M-M	DMF	88	78	59 000	2.15	+11.2	118	286
3	MA-(L)-M-M	PhCl	100	91	73 000	3.12	+11.7	120	286
4	MA-(D)-M-M	PhCl	97	94	61 000	2.70	-11.6	126	295
5	MA-(L,D)-M-M	PhCl <sup>d</sup>	94	89	82 000	2.08	0.0	137	291
6	MA-(L)-M <sub>SO</sub> -M	DMF	100	91	47 000	1.92	-28.1	121	235
7	MA-(L)-M <sub>SO</sub> -M	PhCl	100	92	91 000	2.48	-28.8	119	227
8	MA-(L)-M <sub>SO<sub>2</sub></sub> -M	DMF	96	87	62 000	2.65	-23.1	138	282
9	MA-(L)-M <sub>SO<sub>2</sub></sub> -M	PhCl	100	90	78 000	3.21	-23.5	143	275

Conditions: initiator AIBN 3 mol%, solvent 2 M, 60°C, 20 h  
<sup>a</sup>0.73 M

<sup>b</sup>Estimated by <sup>1</sup>H n.m.r.

<sup>c</sup>Ether-insoluble part

<sup>d</sup>Estimated by g.p.c. based on polystyrene standards; eluent, LiBr solution in DMF (5.8 mM)

<sup>e</sup>Measured by a polarimeter at 27°C (*c* 1.00, DMF)

<sup>f</sup>Determined by d.s.c.

<sup>g</sup>Determined by t.g.a. under nitrogen

**Table 2** Oxidation of poly(MA-(L)-M-M) by hydrogen peroxide

Run	H <sub>2</sub> O <sub>2</sub> (Eq.)	Yield <sup>a</sup> (%)	Unit ratio <sup>b</sup> (mol%)			$\bar{M}_n$ <sup>c</sup>	$\bar{M}_w/\bar{M}_n$ <sup>c</sup>	$[\alpha]_D^{25}$ (°)	$T_g^e$ (°C)	$T_{d10}^f$ (°C)	Refractive index <sup>g</sup>
			-S-	-SO-	-SO <sub>2</sub> -						
1	1	92	87	13	0	93 000	2.77	-26.7	111	236	1.60
2	2	89	0	100	0	85 000	2.34	-30.8	105	238	1.57
3	5	85	0	42	58	85 000	2.36	-27.6	132	245	1.56
4	10	98	0	0	100	87 000	2.60	-24.6	131	282	1.60
5	20	96	0	0	100	78 000	3.38	-25.5	130	280	1.59

Conditions: solvent CHCl<sub>3</sub> (1 M); room temperature, 24 h. Poly(MA-(L)-M) with  $\bar{M}_n$  78 000,  $\bar{M}_w/\bar{M}_n$  3.14,  $[\alpha]_D^{25}$  + 11.7°, RI 1.66 was used

<sup>a</sup>Ether-insoluble part

<sup>b</sup>Estimated by <sup>1</sup>H n.m.r.

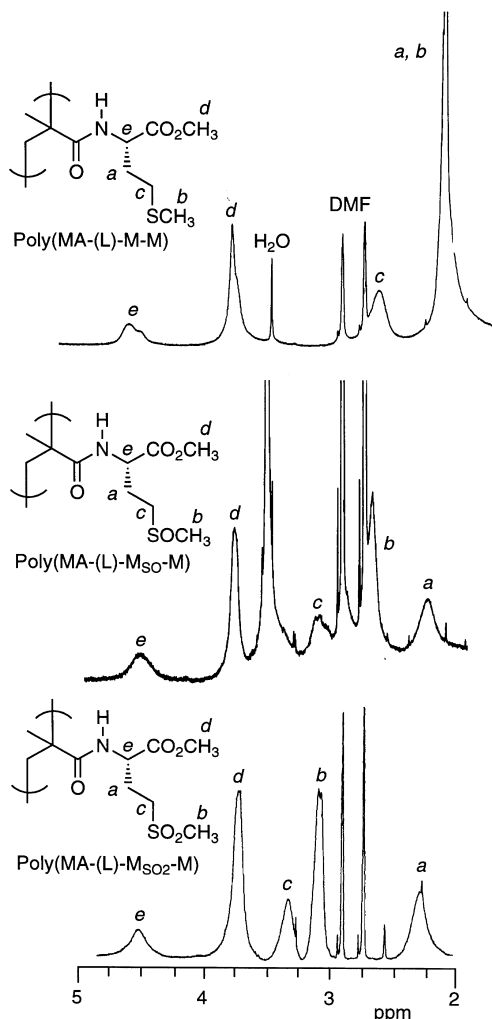
<sup>c</sup>Estimated by g.p.c. based on polystyrene standards; eluent, LiBr solution in DMF (5.8 mM)

<sup>d</sup>Measured by a polarimeter at 25°C (*c* 1.00, DMF)

<sup>e</sup>Determined by d.s.c.

<sup>f</sup>Determined by t.g.a. under nitrogen

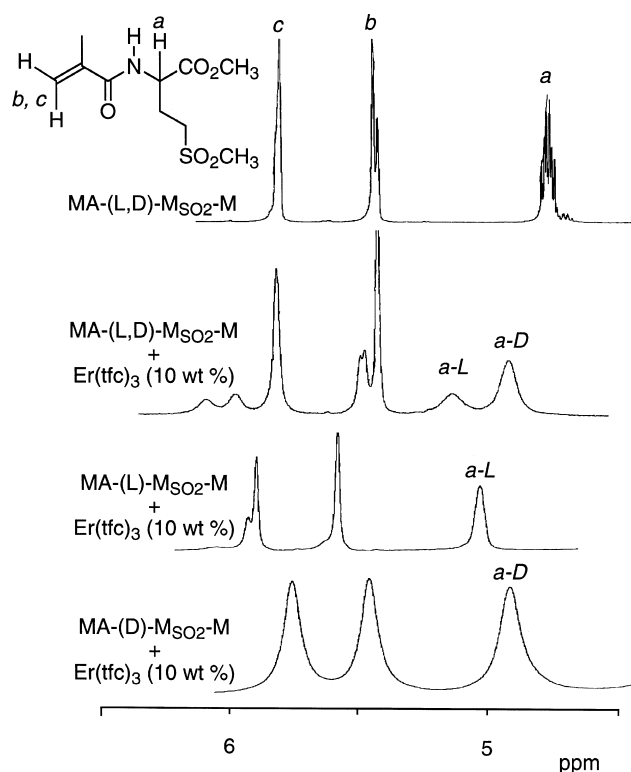
<sup>g</sup>Measured by an Abbe's refractometer



**Figure 1**  $^1\text{H}$  n.m.r. spectra (400 MHz, solvent  $\text{DMF}-d_7$ ) of poly(MA-(L)-M-M), poly(MA-(L)- $\text{M}_{\text{SO}}\text{-M}$ ), and poly(MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ ). Poly(MA-(L)- $\text{M}_{\text{SO}}\text{-M}$ ) and poly(MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ ) were obtained by the oxidations of poly(MA-(L)-M-M) (runs 2 and 5 in Table 2)

sulfur atom. The  $\alpha$ -proton signals shifted to a lower field from sulfide, sulfoxide, and sulfone, as shown in Figure 1. Characteristic i.r. absorption peaks were observed at  $1005\text{ cm}^{-1}$  for the sulfoxide polymer, and  $1296$  and  $1132\text{ cm}^{-1}$  for the sulfone polymer. Poly(MA-(L)-M-M) was selectively oxidized to poly(MA-(L)- $\text{M}_{\text{SO}}\text{-M}$ ) with two equivalents of  $\text{H}_2\text{O}_2$ , and was oxidized to poly(MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ ) with more than 10 equivalents of  $\text{H}_2\text{O}_2$ . The  $\bar{M}_n$  of the polymer increased from 78 000 to 85 000–87 000 after oxidation to the sulfoxide and sulfone polymers. Meanwhile, the model compound of the monomer unit of poly(MA-(L)-M-M), pivaloyl-(L)-M-M was oxidized to the corresponding sulfone compound [pivaloyl-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ ] with two equivalents of  $\text{H}_2\text{O}_2$  (similar conditions in run 2 in Table 2) quantitatively. It is concluded that poly(MA-(L)-M-M) is much hardly oxidized compared to the model compound, probably due to the steric hindrance based on the polymer main chain.

The  $[\alpha]_{\text{D}}^{\text{s}}$  and  $T_g$ s of the sulfoxide and sulfone polymers, obtained by the oxidations of poly(MA-(L)-M-M), showed nearly the similar values with those obtained by the polymerizations of MA-(L)- $\text{M}_{\text{SO}}\text{-M}$  and MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ . Poly(MA-(L)-M-M) showed the largest refractive index value. Table 3 summarizes the solubilities of poly(MA-(L)-M-M), poly(MA-(L)- $\text{M}_{\text{SO}}\text{-M}$ ), and poly(MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ )



**Figure 2**  $^1\text{H}$  n.m.r. spectra (400 MHz, solvent  $\text{DMF}-d_7$ ) of MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ , MA-(D)- $\text{M}_{\text{SO}_2}\text{-M}$ , and MA-(L,D)- $\text{M}_{\text{SO}_2}\text{-M}$  measured in the absence and presence of 10 wt% of Erbium tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorate] ( $\text{Er}(\text{tfc})_3$ )

**Table 3** Solubilities of the polymers

Polymer	Solvent				
	$\text{CHCl}_3$	$\text{CH}_2\text{Cl}_2$	DMF	DMSO	$\text{H}_2\text{O}$
Poly(MA-(L)-M-M)	+	+	+	–	–
Poly(MA-(L)- $\text{M}_{\text{SO}}\text{-M}$ )	–	–	+	–	–
Poly(MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ )	–	–	+	+	–

+ , Soluble at room temperature; – , insoluble at room temperature

in solvents. Poly(MA-(L)-M-M) was soluble in  $\text{CHCl}_3$ ,  $\text{CH}_2\text{Cl}_2$ , and DMF but insoluble in DMSO and  $\text{H}_2\text{O}$ . Poly(MA-(L)- $\text{M}_{\text{SO}}\text{-M}$ ) was only soluble in DMF, and poly(MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ ) was soluble in DMF and DMSO. Poly(MA-(L)- $\text{M}_{\text{SO}}\text{-M}$ ) showed a lower solubility than poly(MA-(L)-M-M) and poly(MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ ) similar to the other sulfoxide polymer<sup>32</sup>.

#### Examination of racemization during oxidation

Racemization during the oxidation of MA-(L)-M-M was examined by  $^1\text{H}$  n.m.r. spectroscopy in the presence of an optically active shift reagent. Figure 2 illustrates the  $^1\text{H}$  n.m.r. spectra of MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$ , MA-(D)- $\text{M}_{\text{SO}_2}\text{-M}$ , and MA-(L,D)- $\text{M}_{\text{SO}_2}\text{-M}$  measured in  $\text{DMF}-d_7$  in the absence and presence of 10 wt% of Erbium tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorate] ( $\text{Er}(\text{tfc})_3$ ). MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$  and MA-(D)- $\text{M}_{\text{SO}_2}\text{-M}$  were synthesized by the oxidations of MA-(L)- and MA-(D)-M-M using hydrogen peroxide, respectively. By the addition of  $\text{Er}(\text{tfc})_3$ , the asymmetric methine proton signal (a) of MA-(D,L)- $\text{M}_{\text{SO}_2}\text{-M}$  split into two (a-L and a-D), each of which was assignable to the methine proton of MA-(L)- $\text{M}_{\text{SO}_2}\text{-M}$  and MA-(D)- $\text{M}_{\text{SO}_2}\text{-M}$ . No methine proton corresponding to the

enantiomer was observed in the  $^1\text{H}$  n.m.r. spectra of MA-(L)-M<sub>SO<sub>2</sub></sub>-M and MA-(D)-M<sub>SO<sub>2</sub></sub>-M in the presence of Er(tfc)<sub>3</sub>. Thus, it may be concluded that no racemization takes place during the oxidation from MA-(L)-M-M to MA-(L)-M<sub>SO<sub>2</sub></sub>-M, and MA-(D)-M-M to MA-(D)-M<sub>SO<sub>2</sub></sub>-M. It can be assumed that no racemization proceeds during the oxidation of poly(MA-(L)-M-M) from this result.

## SUMMARY

In this paper, syntheses and radical polymerizations of methacrylamides having methionine, methionine sulfoxide, and methionine sulfone moieties were carried out. Further, oxidations of the polymethacrylamide having a methionine moiety were examined. The radical polymerizations of the monomers afforded the corresponding polymers using AIBN as an initiator in good yields. The polymer was oxidized by hydrogen peroxide in CHCl<sub>3</sub> (1 M) at room temperature for 24 h. The oxidations by two and ten equivalents of hydrogen peroxide selectively afforded the polymers having methionine sulfoxide and sulfone structures in the side chains, respectively. Further, syntheses and radical polymerizations of methacrylamides having methionine sulfoxide and sulfone moieties in the side chains were carried out. Little differences were observed in the T<sub>g</sub>s and specific rotations between the polymers obtained by their radical polymerizations and the polymers obtained by the oxidation of the polymethacrylamide having a methionine moiety.

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