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(14) See ref 5, in which it has been reported that the analogous polyhydrocarbon, however, whose spacer groups are ethylene and whose distyrylbenzene groups consist of both cis and trans stereoisomers along with a chloro substituent, shows liquid crystallinity.

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Radical Copolymerization of Lipoamide with Vinyl Monomers

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ABSTRACT: Lipoamide, which is a five-membered cyclic disulfide, was copolymerized with some vinyl monomers (styrene, vinyl acetate, acrylonitrile, and methyl acrylate) by 2,2′-azobis(isobutyronitrile) as a radical initiator at 82 °C for 2 h in benzene to give copolymers with sulfide linkages in the main chain and various functional groups as pendants in good yield. The copolymerization might proceed by chain-transfer-type attacking of the propagating vinyl polymer radical at the S–S bond of lipoamide.

Introduction

Lipoamide (LAm), a five-membered cyclic disulfide, works as a coenzyme in the oxidative acyl transfer reaction in living systems. We have already investigated the application of its acyl transfer and redox character to organic synthesis.[1,2]

On the other hand, cyclic disulfides copolymerize with vinyl monomers by homolytic reactions. For example, styrene[3] and vinyl acetate[4] copolymerize with 1-oxa-3,4-dithiacycloheptane (a seven-membered cyclic disulfide) by chain transfer of their propagating polymer radicals to cyclic disulfides to give polymers with sulfide linkages in the main chain. By ultraviolet irradiation, a disulfide linkage of trimethylene disulfide (a five-membered cyclic disulfide) is cleaved to form thiyl radicals and polymerized.[5] Then cyclic disulfides are attractive as comonomers in radical polymerization. We have already reported thermal and photoinitiated copolymerization of LAm with styrene without initiators.[6]

In this paper, we describe the copolymerization of LAm, which is a cyclic disulfide having an amide group, with vinyl monomers, i.e., styrene (St), methyl methacrylate (MMA), vinyl acetate (VAc), acrylonitrile (AN), and methyl acrylate (MA), in the presence of 2,2′-azobis(isobutyronitrile) as a radical initiator. For comparison, we report the synthesis of 4,4′-bis[(benzoyloxy)methyl]-1,2-dithiolane (BDT), which is a five-membered cyclic disulfide without an amide group, and its copolymerization with styrene.

Experimental Section

Materials. Lipoamide (LAm) was supplied by Fujisawa pharmaceutical Co. Ltd. and recrystallized from acetonitrile. Vinyl monomers and solvents were purified by the usual procedure.

Measurements. IR spectra were recorded on a JASCO FT/IR-3 spectrophotometer. ^{1}H NMR spectra were recorded on a JNM-FX 100 FT NMR and a JEOL PMX-60 spectrometer. GPC measurement of polymers in tetrahydrofuran (THF) was carried out with a TOYO SODA HPLC CCCP&8000 system equipped with polystyrene gel columns (TSK gel G2000H, G2500H, and G3000H). The number-average molecular weight ($\bar{M}_n$) and the weight-average molecular weight ($\bar{M}_w$) were calculated on the basis of polystyrene.

Copolymerization of LAm with Vinyl Monomers. Typical procedure: LAm (0.306 g, 1.49 mmol), St (0.879 g, 8.44 mmol), 2,2′-azobis(isobutyronitrile) (AIBN) (32.6 mg, 0.199 mmol), and dimethyl sulfoxide (DMSO) (2.34 mL) were charged into a Pyrex tube and the solution was degassed. The copolymerization was carried out in a sealed tube at 82 °C for 2 h with stirring. After the reaction, the reaction solution was diluted with chloroform and the polymer was precipitated with methanol, separated by filtration, and dried in vacuo. A white powdery copolymer was obtained (0.586 g, 49.4%). ^{1}H NMR ($CDCl_3$) δ 0.8–3.0 (CH_2, CH), 3.3 (CHS), 5.3 ($CONH_2$), and 6.3–7.4 ppm (Ph); IR (KBr) 3400, 3500 (NH_2), 1674 ($CONH_2$), 1602, 1494, and 698 cm^{-1} (Ph). The content of LAm in the copolymer was estimated by ^{1}H NMR to be 7.8 mol %.

The copolymerization of LAm with other comonomers was carried out by the same procedure as above.

When MMA was used as a comonomer, the copolymerization did not proceed and homopolymer of MMA alone was obtained.

When MA was used as a comonomer, the resulting copolymer was precipitated with ether, separated by decantation, and dried in vacuo to obtain a colorless viscous polymer in 88.4% yield. The content of LAm, 11.9 mol %; ^{1}H NMR ($CDCl_3$) δ 1.0–2.6 (CH_2, CH), 2.7 (CHS), 3.7 (CH_3), and 5.8 ppm ($CONH_2$); IR (KBr) 3200, 3370 ($CONH_2$), 1740 (COO), 1660, 1630 ($CONH_2$), and 1166 cm^{-1} ($COOCH_3$).

When VAc was used as a comonomer, a colorless viscous copolymer was obtained in 77.7% yield. ^{1}H NMR ($CDCl_3$) δ 1.2–2.3 (CH_2), 2.0 (CH_3), 2.5–3.1 (CHS, SCH_2), 4.9 (CHO), and 6.0 ppm ($CONH_2$); IR (KBr) 3450 (NH_2), 1740 (COO), 1668, 1628 ($CONH_2$), and 1240 cm^{-1} (CH_3COO).

When AN was used as a comonomer, the reaction solution was diluted with *N*,*N*-dimethylformamide (DMF) and the resulting copolymer was precipitated with methanol, separated by

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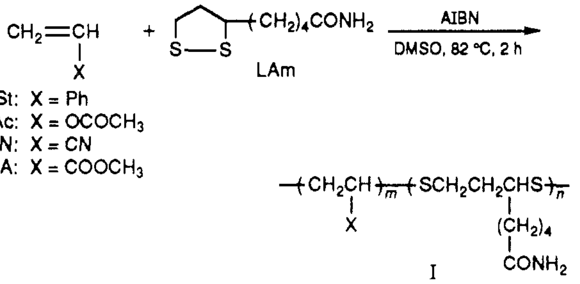
filtration, and dried in vacuo to obtain a pale brown powdery polymer in 81.9% yield. ^{1}H NMR (Me$_2$SO-d_6) δ 1.2–2.4 (CH$_2$), 2.6–3.4 (CHCN, CHS), 6.5 and 7.5 ppm (CONH$_2$); IR (KBr) 3380, 3470 (CONH$_2$), 2250 (CN), 1668, and 1618 cm^{-1} (CONH$_2$).

Preparation of 4,4'-Bis[(benzoyloxy)methyl]-1,2-dithiolane (BDT). 4,4'-Bis(hydroxymethyl)-1,2-dithiolane[7] (1.8 g, 11 mmol) and benzoyl chloride (3.7 g, 26 mmol) were dissolved in THF (63 mL) under a nitrogen atmosphere. To this solution, a THF solution (27 mL) of triethylamine (3.3 g, 33 mmol) was added dropwise and the reaction mixture was refluxed for 17 h with stirring. A white precipitate (Et$_3$N·HCl) was removed by filtration and cyclohexylamine (3.8 g, 39 mmol) was added to remove the excess benzoyl chloride as the corresponding amide. The solution was allowed to stand for 30 min and the solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate, washed with brine and 0.5 N hydrochloric acid, and dried over MgSO$_4$. After filtration, the solvent was evaporated and BDT was isolated (3.2 g, 73%) by column chromatography on silica gel (Wakogel C-200, benzene) and recrystallized from methanol to give yellow needles: mp 90.2–93.4 °C; ^{1}H NMR (CCl$_4$) δ 3.2 (s, 4 H, SSCH$_2$), 4.4 (s, 4 H, COOCH$_2$), 7.2–7.3 (m, 4 H, Ph), and 7.8–8.3 ppm (m, 6 H, Ph); IR (KBr) 1713 (C=O), 1601, and 690 cm^{-1} (Ph). Anal. Calcd for C$_{19}$H$_{18}$O$_4$S$_2$: C, 60.94; H, 4.84; S, 17.13. Found: C, 60.62; H, 4.77; S, 17.39.

Copolymerization of BDT with Styrene. In a typical procedure, BDT (48.6 mg, 0.130 mmol), AIBN (2.9 mg, 0.018 mmol), and St (76.9 mg, 0.738 mmol) were dissolved in benzene (0.205 mL). The solution was degassed and copolymerization was carried out in a sealed Pyrex tube at 80 °C for 2 h. After the polymerization, the reaction solution was diluted with CH$_2$Cl$_2$ and the polymer was precipitated with methanol, separated by filtration, and dried in vacuo. A white powdery copolymer was obtained (67.2 mg, 53.5%). ^{1}H NMR (CDCl$_3$) δ 0.7–2.6 (CH$_2$CHPh, SCH$_2$), 4.1 (OCH$_2$), 6.0–7.6, and 7.6–8.0 ppm (Ph); IR (KBr) 1724 (C=O), 1601, and 698 cm^{-1} (Ph).

Results and Discussion

Copolymerization of LAm with Vinyl Monomers. Copolymerization of LAm with vinyl monomers, i.e., styrene (St), vinyl acetate (VAc), acrylonitrile (AN), methyl acrylate (MA), or methyl methacrylate (MMA), was carried out at 82 °C for 2 h in a sealed tube. The feed ratio of LAm was 15 mol % of the total monomers with a total concentration of 3.0 mol L^{-1} in dimethyl sulfoxide (DMSO), and the amount of AIBN (a radical initiator) was 2.0 mol % of the total monomers. Powdery polymers were obtained in good yield in every case by precipitation with methanol or ether as summarized in Table I.



I (1)

By characterization of the resulting polymers with IR and ^{1}H NMR spectra, St, VAc, AN, and MA were found to give copolymers (I) with LAm, which have sulfide linkages in main chain and various functional groups at side chains, whereas MMA did not copolymerize and only a homopolymer of MMA was obtained. All polymers showed a single peak on their GPC analysis. The polymerization did not proceed without AIBN (Table I, runs 6 and 7), and LAm itself did not polymerize with AIBN (Table I, run 8). These results suggest that copolymerization proceeds as follows (Scheme I). The polymerization is initiated in the same way as the usual vinyl polymerization. Then the propagating radicals attack the cyclic disulfide linkage of LAm by chain-transfer-type reaction to produce macro thiyl radicals.[3,4] And these radicals further attack the vinyl monomer or LAm to form copolymers with the sulfide linkage and to some extent the disulfide linkage in the main chain[6] and functional groups as pendants.

MMA did not copolymerize with LAm but MA and AN did, which suggested that the attack of the propagating radical of MMA on LAm was inhibited by steric hindrance of the methyl group in the propagating poly(MMA) radical.

The yield of copolymers decreases in the order MA > AN > VAc > St (Table I), and that of homopolymerization of MA, VAc, or St decreases in the same order (Table II). Thus the yield of copolymers depended on the reactivity of comonomers. When St was copolymerized with LAm, the $\bar{M}_n$ of the copolymer was comparatively high. In the case of copolymerization of MA and VAc with LAm, the $\bar{M}_n$ of the copolymers decreased dramatically com-

Table I
Copolymerization of LAm with Vinyl Monomers^a

run	co-monomer	AIBN, mol %	yield,^{b} %	copolymer comp, mol %^{d} m:n	$\bar{M}_n$^{e}	$\bar{M}_w$/$\bar{M}_n$^{e}
1	St	2.0	49.4	92.9:7.8	10 570	1.42
2	VAc	2.0	77.7^c	75.1:24.9	2 210	3.15
3	AN	2.0	81.9	90.6:9.4	52 190^f	1.39^f
4	MA	2.0	88.4^c	88.1:11.9	2 910	1.81
5	MMA	2.0	54.2	100:0	15 470	1.70
6	St		0			
7	MMA		0			
8		2.0	0			

^{a} Monomers, 3.0 mol·L^{-1} in DMSO; vinyl monomer: LAm = 85:15 (molar ratio); reaction temperature, 82 °C; reaction time, 2 h. ^{b} Precipitated with methanol. ^{c} Precipitated with ether. ^{d} Estimated by ^{1}H NMR. ^{e} Estimated by GPC analysis in THF on the basis of polystyrene calibration. ^{f} Estimated by GPC analysis in 10 mM LiBr DMF solution on the basis of polystyrene calibration.

Scheme I

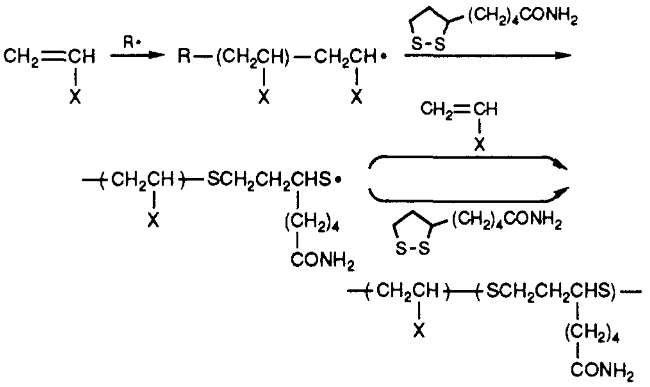


Table II
Homopolymerization of Vinyl Monomers^a

run	monomer	AIBN, mol %	yield, %	$\bar{M}_n$^{d}	$\bar{M}_w$/ $\bar{M}_n$^{d}
9	St	2.4	57.1^b	7 720	1.53
10	VAc	2.4	90.4^c	17 360	1.95
11	MA	2.4	91.3^c	19 460	4.33

^{a} Vinyl monomers, 2.6 mol·L^{-1} in DMSO; reaction temperature, 82 °C; reaction time, 2 h. ^{b} Precipitated with methanol. ^{c} Precipitated with ether. ^{d} Estimated by GPC analysis in THF on the basis of polystyrene calibration.

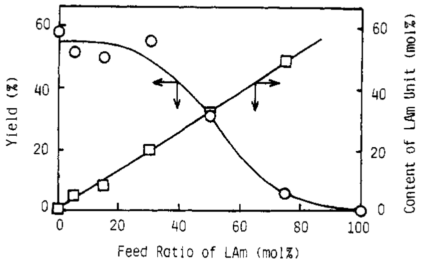


Figure 1. Effect of the feed ratio of comonomers on yields and contents of the LAm unit in copolymers in the copolymerization of LAm with St. Monomers, 3.0 mol·L^{-1} in DMSO; AIBN, 2.0 mol %; at 82 °C for 2 h.

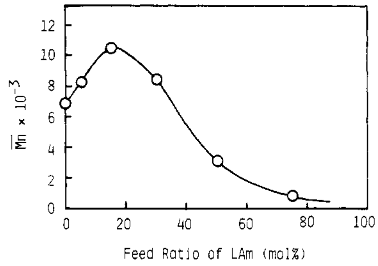


Figure 2. Effect of the feed ratio of comonomers on $\bar{M}_n$ in the copolymerization of LAm with St. Monomers, 3.0 mol·L^{-1} in DMSO; AIBN, 2.0 mol %; at 82 °C for 2 h. Estimated by GPC analysis in THF on the basis of polystyrene calibration.

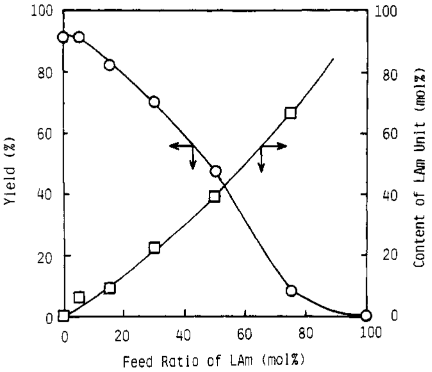


Figure 3. Effect of the feed ratio of comonomers on yields and contents of the LAm unit in the copolymers in the copolymerization of LAm with AN. Monomers, 3.0 mol·L^{-1} in DMSO; AIBN, 2.0 mol %; at 82 °C for 2 h.

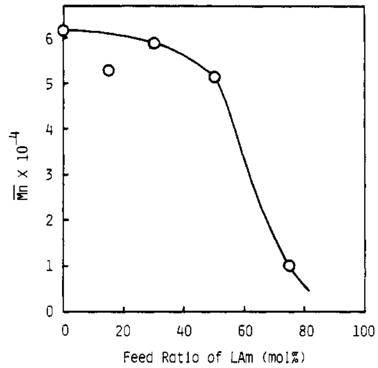


Figure 4. Effect of the feed ratio of comonomers on $\bar{M}_n$ in the copolymerization of LAm with AN. Monomers, 3.0 mol·L^{-1} in DMSO; AIBN, 2.0 mol %; at 82 °C for 2 h. Estimated by GPC analysis in 10 mM LiBr DMF solution on the basis of polystyrene calibration.

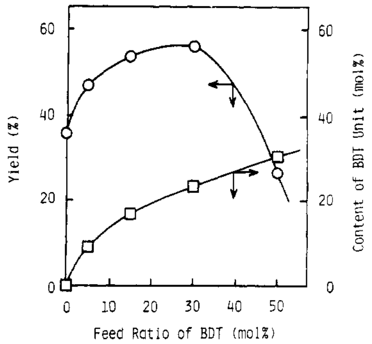


Figure 5. Effect of feed ratio of comonomers on yields and contents of the BDT unit in copolymers in the copolymerization of BDT with St. Monomers, 3.0 mol·L^{-1} in benzene; AIBN, 2.0 mol %; at 80 °C for 2 h.

pared with those of the corresponding homopolymers (Tables I and II). With reference to the available chain-transfer constants of St to di-*n*-butyl disulfide (0.026) and to di-*n*-butyl sulfide (0.0022)[8] and those of VAc to di-*n*-butyl disulfide (1.0) and di-*n*-butyl sulfide (0.026)[4] at 60 °C, the formation of the VAc copolymer with a higher content of LAm and a lower $\bar{M}_n$ having a wider distribution is explained by the comparatively higher reactivity of VAc polymer radical to LAm and the sulfide groups formed in the resulting copolymer chain.

Copolymerization of LAm with St. Only in the case of copolymerization of LAm with St, the $\bar{M}_n$ of the copolymer was higher than that of polystyrene. Then copolymerization of LAm with St was further investigated by varying the feed ratio of LAm to St.

The yield was almost constant (50–60%) in the range 0–30 mol % of the feed ratio of LAm and decreased greatly by increasing the ratio to more than 30 mol % as shown in Figure 1. The $\bar{M}_n$ of the copolymers increased by increasing the feed ratio of LAm, reached a maximum ($\bar{M}_n$ = 10 570) when the feed ratio of LAm was 15 mol %, and decreased as the feed ratio increased (Figure 2). In the copolymerization of LAm with St, it is roughly concluded that the attack of the macro thiyl radical, formed by the reaction of a styryl polymer radical with LAm, on St is not as great a disadvantage as in the other polymerization cases due to the resonance stabilization in the formation of styryl radicals. The decrease of yield and $\bar{M}_n$ at the higher feed ratio would be caused by the lower reactivity of macro thiyl radicals than that of the propagating St polymer radicals. Further disulfide bonds formed by the reaction of macro thiyl radicals with LAm might be more susceptible to radical attacking than sulfide linkage.

Copolymerization of LAm with AN. For comparison, the copolymerization of LAm with AN was carried out by varying the feed ratio of LAm.

As the feed ratio increased, the yield and $\bar{M}_n$ decreased and the content of LAm in the copolymer increased continuously (Figures 3 and 4). The yield and the content of LAm in the copolymer were larger than those of copolymers with St. This is caused by the higher reactivity of the propagating AN polymer radical to LAm than the St polymer radical.

Copolymerization of 2,2-Bis[(benzoyloxy)methyl]-1,2-dithiolane (BDT) with St. In radical polymerization, chain transfer to amide groups is susceptible. In order to investigate the effect of an amide group on copolymerization, 2,2-bis[(benzoyloxy)methyl]-1,2-dithiolane (BDT) was synthesized by esterification of the corresponding diol[7] as a reference compound of LAm and copolymerized with St. BDT is stable in air and has a good solubility in some organic solvents.

Copolymerization was carried out in benzene at 80 °C for 2 h by varying the feed ratio of BDT to the total monomers from 5 to 50 mol % with a total concentration of 3.0 mol L^{-1}. AIBN (2.0 mol %) was used as an

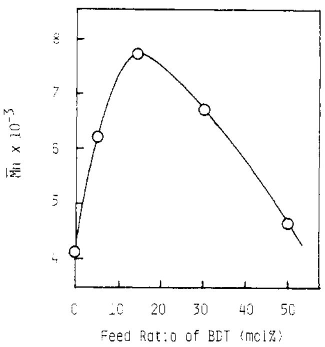
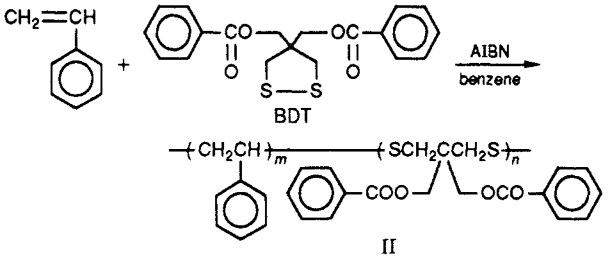


Figure 6. Effect of feed ratio of comonomers on $\bar{M}_n$ in copolymerization of BDT with St. Monomers, 3.0 mol·L^{-1} in benzene; AIBN, 2.0 mol %; at 80 °C for 2 h. Estimated by GPC analysis in THF on the basis of polystyrene calibration.

initiator. Copolymer II was precipitated with methanol and isolated. The structures of the copolymers was confirmed by IR and ^{1}H NMR spectra. All copolymers showed one peak by GPC analysis.



(2)

BDT itself did not polymerize at all with AIBN. Thus in the case of BDT, a copolymer was also formed by attack of propagating vinyl polymer radical on the disulfide linkage of BDT.

As the feed ratio of BDT increased from 0 to 30 mol %; the yield of copolymer II increased (Figure 5) and decreased greatly as the feed ratio of BDT increased from 30 to 50 mol %. The content of BDT in copolymer II increased as the feed ratio of BDT increased. The $\bar{M}_n$ of the copolymers gave a maximum ($\bar{M}_n$ = 7740) when the feed ratio of BDT was 15 mol % (Figure 6). These observations are similar to that of copolymerization of LAm with St and indicate that copolymerization is little affected by the amide group.

In summary, in the presence of a radical initiator, five-membered cyclic disulfides were copolymerized with vinyl monomers St. VAc, AN, and MA but not with MMA. Since the cyclic disulfide itself did not homopolymerize, it was concluded that vinyl polymerization was initiated by attack of the radical species produced from AIBN on vinyl monomers, and the copolymer was formed by a chain-transfer-type reaction of the propagating vinyl polymer radical with the cyclic disulfide linkage.

This copolymerization proceeds under mild conditions in good yield and is useful for the synthesis of a polymer with sulfide linkages in the main chain and various functional groups as pendants.

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Registry No. (LAm)(St) (copolymer), 125049-63-0; (LAm)(MA) (copolymer), 125049-64-1; (LAm)(VAc) (copolymer), 125049-65-2; (LAm)(AN) (copolymer), 125049-66-3; BDT, 125049-62-9; (BDT)(St) (copolymer), 125049-67-4.