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Radical Polyadditions of Dithiols with Diolefins Derived from Optically Active Amino Alcohols

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ABSTRACT: Syntheses of poly(ester-amide-sulfide)s by radical polyadditions of diolefins with dithiols and oxidations and enzymatic degradation of the obtained polymers were examined. The diolefins were synthesized from optically active amino alcohols and 4-pentenoic acid. The radical polyadditions of the diolefins with dithiols were carried out in the presence of AIBN (3 mol %) in DMF to afford high molecular weight polymers. The sulfide group in the polymer was selectively oxidized to sulfoxide and sulfone groups according to the amount of H_2O_2 used. The poly(ester-amide-sulfide)s derived from alaninol were degraded by lipase *Rhizopus arrhizus*.

Introduction

Amino acids are constituents of proteins, are typical biological polymers, and are not only biologically related but also useful substances for chiral auxiliaries and building blocks in organic synthesis. Polypeptides consisting of amino acids have been examined as models of proteins that show a variety of chemical and biochemical functions. Synthetic polymers based on amino acids are also expected to show biodegradability.[1] A poly(ester-carbamate) obtained by the condensation of phenylalanine (2-hydroxyethyl)carbamate is hydrolyzed by tripsin.[2] Poly(ester-amide)s obtained by the condensations of disuccinimidyl adipate and diamines derived from amino acids and ethylene glycol are hydrolyzed by chymotrypsin.[3] β-Amino alcohols obtained by reduction of amino acids are also useful compounds in the field of biochemistry and organic chemistry and can serve as ligands where the heteroatoms form a complex with a metal. A chiral β-amino alcohol catalyzes enantioselective conjugate addition of diethylzinc to enone.[4] A large number of natural products contain the amino alcohol functionality such as amino sugar and nucleosides. We have reported the syntheses of several novel polymers derived from optically active amino alcohols by polycondensations and radical polymerizations.[5] In this paper, we describe syntheses of novel poly(ester-amide-sulfide)s by radical polyadditions of dithiols with diolefins derived from optically active amino alcohols and 4-pentenoic acid and oxidations of the poly(ester-amide-sulfide)s to poly(ester-amide-sulfoxide)s and poly(ester-amide-sulfone)s. Polysufoxides are noteworthy, because they are applicable as the polymeric oxidant and selective permeation membrane for isolation of SO_2, etc.[6] The obtained poly(ester-amide-sulfide)s contain ester and amide groups in the polymer main chains, which are susceptible to hydrolysis. Therefore, enzymatic degradation of the poly(ester-amide-sulfide)s with lipase *Rhizopus arrhizus* is also evaluated.

Experimental Section

Measurements. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM EX-90 and EX-400 spectrometers using tetramethylsilane (TMS) as an internal standard in chloroform-*d* ($CDCl_3$) or dimethyl sulfoxide-d_6 (DMSO-d_6). IR spectra were obtained with a JASCO FT/IR-5300. Melting points (mp) were measured by a Yanaco micro melting point apparatus. Specific rotations ($[\alpha]_D$) were measured on a JASCO DIP-1000 digital polarimeter using a sodium lamp as a light source. Elemental analyses were performed on a Yanaco CHN Corder MT-5. Number and weight average molecular weights ($\bar{M}_n$ and $\bar{M}_w$, respectively) and the polydispersity ratios ($\bar{M}_w/\bar{M}_n$) were estimated by gel permeation chromatography (GPC) on a Tosoh HPLC HLC-8020 system, equipped with four polystyrene gel columns (TSK gel, G6000H, G5000H, G4000H, and G2500H), using *N,N*-dimethylformamide (DMF, 5.8 mM lithium bromide solution) as an eluent at a flow rate 1.0 mL/min, a polystyrene calibration, and refractive index (RI) and ultraviolet (UV) detectors. Thermal analyses were performed on Seiko Instruments TG/DTA220 and DSC220C. The glass transition temperature (T_g) was taken as an inflection point on a trace by differential scanning calorimetry (DSC) at a heating rate of 10 °C/min. 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. Compounds 4-pentenoic acid (Aldrich Chemical Co.), 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide hydrochloride (EDC·HCl, Eiweiss Chemical Co.), 4-(dimethylamino)pyridine (DMAP, Tokyo Kasei Kogyo Co.), 2,2′-azobis(isobutyronitrile) (AIBN, Tokyo Kasei Kogyo Co.), H_2O_2 (31% aqueous solution), 3-chloroperoxybenzoic acid (*m*-CPBA, 80%, Tokyo Kasei Kogyo Co.), and lipase *Rh. arrhizus* (Sigma, lipase type XI from *Rh. arrhizus* suspension in 3.2 M $(NH_4)_2SO_4$−10 mM potassium phosphate solution) were used as received. All thiols and dithiols (Aldrich Chemical Co.) were distilled before use. DMF was distilled over calcium hydride. Amino alcohols were synthesized by the reduction of the corresponding amino acid methyl ester hydrochlorides with lithium aluminum hydride. The $[\alpha]_D$ values of the amino alcohols obtained agreed well with the reported ones[7].

Syntheses of Diolefins. DPA-A. To a solution of 4-pentenoic acid (8.51 g, 85 mmol) and EDC·HCl (16.29 g, 85 mmol) in CH_2Cl_2 (80 mL) was added L-alaninol (3.00 g, 40 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h, and DMAP (0.98 g, 8.0 mmol) was added to the mixture followed by stirring at room temperature overnight. The reaction mixture was washed with water, aqueous sodium hydrogen carbonate, and water. After the organic phase was concentrated by rotary evaporation, the residue was purified by silica gel column chromatography (eluent: ethyl acetate−*n*-hexane 1:1) to afford a colorless oil in 76% yield; $[\alpha]^{23}_D = -7.4°$ ($c = 1$, DMF). ^{1}H NMR ($CDCl_3$): δ 1.16 (d, $J = 6.7$ Hz, 3 H, $>CHCH_3$),

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2.25−2.50 (m, 8 H, CH$_2$=CH(CH$_2$)$_2$−), 4.02−4.09 (m, 2 H, −CH$_2$OC(=O)−), 4.09−4.50 (m, 1 H, >CHCH$_2$−), 4.90−5.20 (m, 4 H, CH$_2$=CH−), 5.60−6.20 (m, 3 H, CH$_2$=CH−, NH). ^{13}C NMR (CDCl$_3$): δ 11.48, 12.37, 16.10, 18.42, 26.92, 49.53, 98.09, 98.26, 119.28, 119.74, 154.73, 155.64. IR (KBr): 3277, 3079, 2980, 1740, 1644, 1547, 1451, 1377, 1267, 1175, 995, 916 cm^{-1}. Anal. Calcd for $C_{13}H_{21}NO_3$: C, 65.25; H, 8.84; N, 5.85. Found: C, 65.19; H, 8.94; N, 5.55.

DPA-L and DPA-F. The title compounds were synthesized similarly to DPA-A. The analytical data are included in the Supporting Information.

Model Reactions. Adduct of DPA-F with Ethanethiol (DPA-F-ET). To DPA-F (157.7 mg, 0.5 mmol) in a reaction tube were introduced AIBN (8.2 mg, 0.05 mmol) and subsequently ethanethiol (124.3 mg, 2.0 mmol) and dry DMF (250 μL). The tube was cooled, degassed, sealed off, and heated at 60 °C for 20 h. After the conversion of DPA-F was determined by ^{1}H NMR, the solvent was evaporated from the reaction mixture. The residue was purified by HPLC (eluent: chloroform) to afford a colorless solid in 85% yield; mp 70 °C (measured by DSC), $[\alpha]^{27}_D = -8.4$ °(c = 1, DMF). ^{1}H NMR (CDCl$_3$): δ 0.98 (m, 3 H, CH$_3$−), 1.50−1.80 (m, 8 H, C(=O)CH$_2$(CH$_2$)$_2$−), 2.10−2.60 (m, −SCH$_2$−, C(=O)CH$_2$−), 2.84 (m, 2 H, −CH$_2$Ph), 4.06 (d, J = 5.2 Hz, 2 H, −CH$_2$OC(=O)−), 4.40−4.50 (m, 1 H, >CHNH−), 5.92 (d, J = 8.8 Hz, 1 H, NH), 7.20−7.32 (m, 5 H, −Ph). ^{13}C NMR (CDCl$_3$): δ 18.55, 36.97, 53.13, 64.31, 119.96, 126.77, 128.72, 129.24, 137.62, 139.81, 169.01. IR (KBr): 3302, 2959, 2888, 1655, 1620, 1545, 1452, 1231, 1055, 922 cm^{-1}. Anal. Calcd for $C_{23}H_{37}NO_3S_2$: C, 62.83; H, 8.48; N, 3.19. Found: C, 62.63; H, 7.78; N, 3.13.

The other adducts of DPA-F with the other thiols were synthesized similarly to DPA-F-ET. The analytical data are included in the Supporting Information.

Radical Polyaddition. Typical Procedure. To a diolefin (3.00 mmol) and a dithiol (3.00 mmol) in a polymerization tube were introduced AIBN (0.015 mg, 0.09 mmol) and subsequently dry DMF (3 mL). The tube was cooled, degassed, sealed off, and heated at 60 °C for 24 h. After the conversion of the diolefin was determined by ^{1}H NMR, the reaction mixture was poured into ether to precipitate a polymer. The ether-insoluble polymer was centrifuged to remove the supernatant and dried at 60 °C in vacuo overnight.

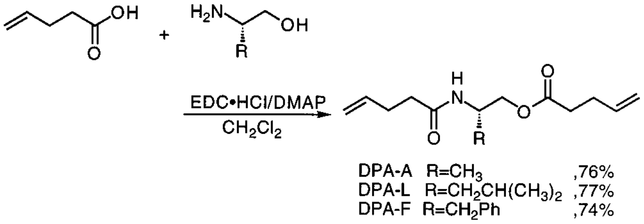
Poly(DPA-A-EDT). ^{1}H NMR (CDCl$_3$): δ 1.17 (d, J = 6.4 Hz, 3 H, CH$_3$−), 1.60−1.90 (m, 8 H, −C(=O)CH$_2$(CH$_2$)$_2$−), 2.19 (t, J = 6.8 Hz, 2 H, −NHC(=O)CH$_2$−), 2.37 (t, J = 7.2 Hz, 2 H, −OC(=O)CH$_2$−), 2.55 (t, J = 6.4 Hz, 4 H, −SCH$_2$(CH$_2$)$_3$C(=O)−), 2.70−2.80 (m, 4 H, −S(CH$_2$)$_2$S−), 4.00−4.20 (m, 2 H, −CH$_2$OC(=O)−), 4.24−4.40 (m, 1 H, >CHNH−), 5.84 (broad s, 1 H, NH). ^{13}C NMR (CDCl$_3$): δ 17.45, 23.99, 24.84, 29.02, 29.19, 31.86, 32.21, 33.65, 36.19, 44.35, 66.88, 172.13, 173.41. IR (KBr): 3310, 3065, 2930, 2862, 1734, 1645, 1548, 1454, 1379, 1277, 1044 cm^{-1}.

The other polymers were synthesized similarly to poly(DPA-A-EDT). The analytical data are included in the Supporting Information.

Oxidation. Oxidation with H_2O_2. To a solution of poly(DPA-A-HDT) (155.8 mg, 0.4 mmol) in CH$_2$Cl$_2$ (2.0 mL) was added aqueous 31% H$_2$O$_2$ (131.6 mg, 1.2 mmol), and the mixture was vigorously stirred at 25 °C for 24 h. The solvents and residual H$_2$O$_2$ were evaporated from the reaction mixture, and the residue was dried at 60 °C in vacuo; yield 100%, unit molar ratio of sulfide:sulfoxide:sulfone = 2:96:2; $[\alpha]^{23}_D = -3.7°$ (c = 1, DMF). ^{1}H NMR (DMSO-d_6): δ 1.07 (d, J = 6.0 Hz, 3 H, CH$_3$−), 1.40−1.80 (m, 16 H, −C(=O)CH$_2$(CH$_2$)$_2$−, −S(=O)CH$_2$(CH$_2$)$_3$−), 2.08−2.20 (m, 2 H, −NHC(=O)CH$_2$−), 2.30−2.42 (m, 2 H, −OC(=O)CH$_2$−), 2.60−2.80 (m, 8 H, −S(=O)CH$_2$−), 3.90−4.10 (m, 3 H, −CH$_2$OC(=O), >CHNH−), 7.81 (broad s, 1 H, NH). ^{13}C NMR (DMSO-d_6): δ 16.92, 21.69, 21.93, 23.57, 24.49, 27.85, 33.01, 34.67, 43.18, 51.04, 66.20, 171.36, 172.33. IR (KBr): 3267, 3076, 2978, 2944, 2865, 1734, 1647, 1545, 1458, 1416, 1377, 1275, 1179, 1073 cm^{-1}.

Oxidation with *m*-CPBA. To a solution of poly(DPA-A-HDT) (240.2 mg, 0.6 mmol) in CH$_2$Cl$_2$ (6.0 mL) was added *m*-CPBA (80%, 638.3 mg, 3.7 mmol), and the reaction mixture was stirred at 25 °C for 2 days. The oxidized polymer was isolated by precipitation with aqueous sodium hydrogen carbonate and dried at 60 °C in vacuo; yield 90%. ^{1}H NMR (DMSO-d_6): δ 1.03 (d, J = 6.8 Hz, 3 H, CH$_3$−), 1.38−1.78 (m, 16 H, −C(=O)CH$_2$(CH$_2$)$_2$−, −S(=O)$_2$CH$_2$(CH$_2$)$_3$−), 2.08−2.20 (m, 2 H, −NHC(=O)CH$_2$−), 2.30−2.42 (m, 2 H, −OC(=O)CH$_2$−), 3.00−3.16 (m, 8 H, −S(=O)$_2$CH$_2$−), 3.90−4.24 (m, 3 H, −CH$_2$OC(=O), >CHNH−), 7.77 (d, J = 8.0 Hz, 1 H, NH). ^{13}C NMR (DMSO-d_6): δ 16.95, 20.74, 20.81, 23.15, 24.05, 27.19, 32.79, 34.75, 43.18, 51.20, 51.31, 51.48, 66.24, 171.30, 172.49. IR (KBr): 3588, 3314, 2946, 2870, 1732, 1661, 1529, 1462, 1414, 1327, 1285, 1244, 1183, 1123, 1047, 990 cm^{-1}.

Scheme 1



Enzymatic Degradation of the Polymers. Preparation of Enzyme Solution. Received lipase *Rh. arrhizus* in (NH$_4$)$_2$SO$_4$−phosphate buffer (0.08 mL, 400 000 unit) was diluted with pH 7.0 phosphate buffer (0.02 M, 6.0 mL).

Enzymatic Degradation. To a film (20 mg, thickness 70 μm) formed from poly(DPA-A-HDT) by casting from the solution in dichloromethane were added the enzyme solution (0.2 M, 0.2 mL), a phosphate buffer solution (0.2 mL), and water (0.6 mL). The resulting mixture was shaken at 30 °C for a set time. The polymer film was washed by water and dried at 50 °C in vacuo. A percentage weight loss of the polymer film was calculated from the weight of the recovered polymer film. A total organic carbon (TOC) value in the buffer solution was measured after filtration with a membrane filter (pore size 0.2 μm). The residue obtained by evaporation of the buffer solution was analyzed by ^{1}H NMR and IR spectroscopy.

Hydroxy Carboxylic Acid Obtained by the Enzymatic Degradation of Poly(DPA-A-HDT). ^{1}H NMR (DMSO-d_6): δ 1.07 (d, J = 6.8 Hz, 3 H, CH$_3$−), 1.36−1.70 (m, 16 H, −C(=O)CH$_2$(CH$_2$)$_2$−, −SCH$_2$(CH$_2$)$_4$−), 2.15, (t, J = 7.2 Hz, 2 H, −NHC(=O)CH$_2$−), 2.24 (t, J = 6.8 Hz, 2 H, −CH$_2$COOH), 2.42−2.52 (m, 8 H, −SCH$_2$−), 3.30−3.42 (m, 1 H, >CHNH−), 3.80−3.90 (m, 2 H, −CH$_2$OC(=O)−), 7.65 (broad s, 1 H, NH).

Results and Discussion

The diolefins, DPA-A, DPA-L, and DPA-F, were prepared by the condensations of optically active amino alcohols and 4-pentenoic acid using EDC·HCl in satisfactory yields (Scheme 1). The structures of the diolefins were confirmed by ^{1}H and ^{13}C NMR and IR spectroscopy besides elemental analyses.

Radical additions of DPA-F with monofunctional thiols were carried out at 60 °C for 20 h as model reactions for polyadditions in the presence of AIBN (10 mol %) in DMF (2 M) (Scheme 2). The results are shown in Table 1. DPA-F was not converted quantitatively with 2.0 equiv of ethanethiol, probably due to its low boiling point (35 °C), but was converted quantitatively with 2.4 equiv of ethanethiol to afford the corresponding adduct in 85% yield (run 2). DPA-F was converted nearly quantitatively with the other thiols (runs 3−7). The model compounds were isolated by preparative HPLC, and the main structure was confirmed as DPA-F-XT by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy. A small amount (4−6%) of isomers such as DPA-F-XT′ was also formed via an attack by thiols at the α-carbons of the olefin groups of DPA-F.

Radical polyaddition of DPA-F with butanedithiol was carried out with various initiator and monomer concen-

Table 1. Radical Additions of DPA-F with Thiols[a]

run	thiol (R′)	conv of diolefin[b] (%)	yield[c] (%)	mp[d] (°C)	$[\alpha]_D$[e] (deg)	$[M]_D$[f] (deg)
1	CH_3CH_2 (2.0 equiv)	80				
2	CH_3CH_2 (4.0 equiv)	100	85	70	−8.4	−36.9
3	$CH_3(CH_2)_2$ (2.4 equiv)	100	83	58	−9.6	−44.9
4	$CH_3(CH_2)_3$ (2.0 equiv)	94	89	35	−7.9	−39.2
5	$CH_3(CH_2)_4$ (2.0 equiv)	100	82	27	−8.2	−42.9
6	$CH_3(CH_2)_5$ (2.0 equiv)	100	89	29	−7.0	−38.6
7	$C_6H_5CH_2$ (2.0 equiv)	88	79	43	−6.5	−36.6

[a] Conditions: DPA-F concentration, 2 M; solvent in DMF; initiator, AIBN 10 mol %; 60 °C; 20 h. [b] Determined by ^{1}H NMR. [c] Isolated by preparative HPLC. [d] Measured by DSC. [e] Measured by a polarimeter at 26 °C ($c = 1.00$, DMF). [f] Calculated by $[M]_D = [\alpha]_D M_w/100$.

Scheme 2

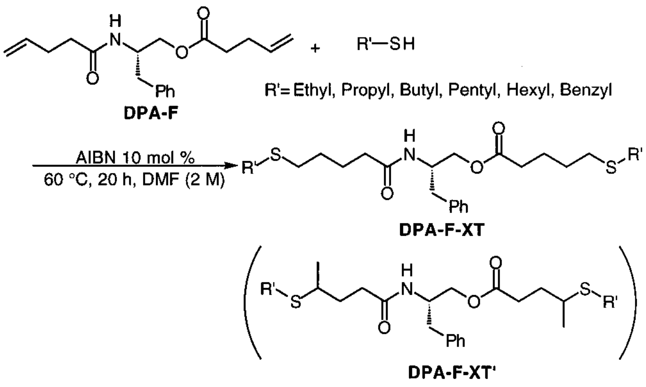
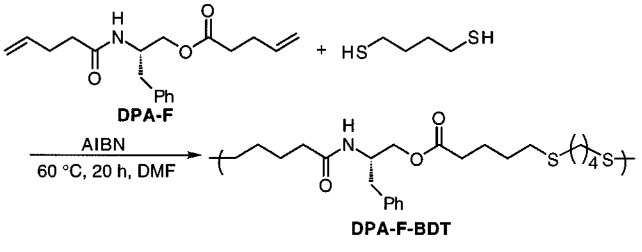


Table 2. Radical Polyaddition of DPA-F with Butanedithiol[a]

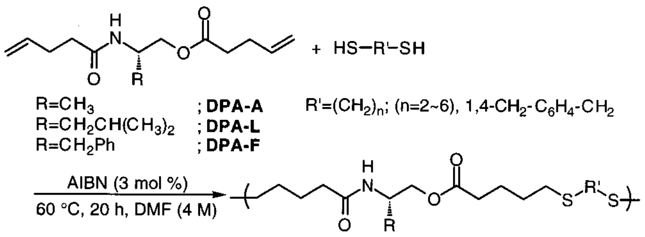
run	AIBN (mol %)	conc of DPA-F[b] (M)	conv of diolefin[c] (%)	yield[d] (%)	$\bar{M}_n(\bar{M}_w/\bar{M}_n)$[e]
1	3	0.1	0	0	
2	3	0.5	85	51	19 500 (1.49)
3	3	1	87	82	19 300 (1.71)
4	3	2	100	95	31 000 (1.50)
5	3	4	100	96	58 300 (1.72)
6	3	10	99	97	52 800 (1.69)
7	3	bulk	83	83	28 800 (1.73)
8	10	2	100	94	50 000 (1.63)
9	10	4	100	96	53 100 (1.71)
10	20	4	100	97	39 000 (1.59)

[a] Conditions: solvent, DMF; 60 °C; 20 h. [b] Calculated by the equation, mmol of DPA-F/mmol of DMF. [c] Determined by ^{1}H NMR. [d] Ether-insoluble part. [e] Estimated by GPC based on polystyrene standards; eluent, LiBr solution in DMF (5.8 mM).

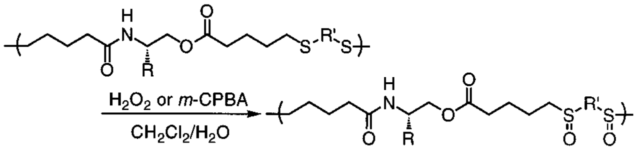
Scheme 3



Scheme 4



Scheme 5



trations, as shown in Table 2. No reaction proceeded with 3 mol % of AIBN in 0.1 M DPA-F concentration (run 1). The yield and $\bar{M}_n$ of the polymer increased to 4 M DPA-F concentration with 3 mol % AIBN (runs 2−5), while they decreased in the polyadditions in 10 M and in bulk (runs 6 and 7), probably due to the high viscosity. The $\bar{M}_n$ of the obtained polymer decreased as the amount of AIBN increased (runs 5, 9, and 10). The structure of the obtained polymer was confirmed as a poly(ester-amide-sulfide) (DPA-F-BDT) by ^{1}H and ^{13}C NMR and IR spectroscopy (Scheme 3). The formation of a small amount (3−8%) of α-adduct structure was confirmed by ^{1}H NMR spectroscopy, similarly to the model reaction.

Radical polyadditions of diolefins (DPA-A, DPA-L, and DPA-F) with several dithiols were carried out at 60 °C for 20 h in the presence of 3 mol % AIBN in DMF (4 M) (Scheme 4). Polymers with $\bar{M}_n$'s of 20 000−75 700 were obtained nearly quantitatively. The structures of the obtained polymers were confirmed by ^{1}H and ^{13}C NMR and IR spectroscopy. The conditions and results of the radical polyadditions are summarized in Table 3. The T_g's of the polymers obtained from ethanedithiol were higher than those of the polymers from the other dithiols, which might reflect the tendency of the melting points of the model compounds as summarized in Table 1.

CD spectra of poly(DPA-F-EDT), poly(DPA-F-PeDT), poly(DPA-F-HDT), and a model compound of the polymers, DPA-F-ET, DPA-F-PeT, and DPA-F-HT, were measured to examine the stereoregularity of the polymers. Since no significant difference was observed for the CD patterns of the polymers and the corresponding model compounds,[8] it may be presumed that no special stereoregularity is present.

The oxidations of the poly(ester-amide-sulfide) [poly(DPA-A-HDT)] obtained from DPA-A and hexanedithiol were carried out with H_2O_2 or *m*-CPBA as an oxidant at room temperature (Scheme 5). The conditions and results are summarized in Table 4. The oxidations with 1.0 equiv of H_2O_2 per sulfide unit, afforded polymers containing the sulfoxide moiety in 43−67% (runs 2−5). Polymers containing the sulfoxide moiety in 83−96% were obtained by the oxidations with 1.5 equiv of H_2O_2 (runs 6−8). Poly(DPA-A-HDT) was completely oxidized to polysulfone with 20 equiv of H_2O_2 and 2.6 equiv of *m*-CPBA (runs 9 and 10). The structures of the oxidized polymers were confirmed by ^{1}H and ^{13}C NMR and IR spectroscopy (Figure 1). Figure 1A illustrates the ^{1}H NMR spectra of poly(DPA-A-HDT) and the oxidized

Table 3. Radical Polyadditions of Diolefins and Dithiols[a]

run	diolefin	dithiol (R′)	conv of diolefin[b] (%)	yield[c] (%)	$\bar{M}_n(\bar{M}_w/\bar{M}_n)$[d]	T_g[e] (°C)	T_{d10}[f] (°C)	$[\alpha]_D$[g]	$[M]_D$[h]
1	DPA-A	$(CH_2)_2$	98	96	61 100 (1.60)	−18	345	−4.0	−13.3
2	DPA-A	$(CH_2)_3$	98	94	36 800 (1.54)	−32	337	−3.7	−12.9
3	DPA-A	$(CH_2)_4$	98	96	62 000 (1.70)	−27	347	−3.5	−12.6
4	DPA-A	$(CH_2)_5$	98	96	53 200 (1.63)	−24	344	−3.3	−12.4
5	DPA-A	$(CH_2)_6$	97	97	48 600 (1.58)	−27	353	−3.4	−13.2
6	DPA-A	1,4-$CH_2C_6H_4CH_2$	97	93	26 100 (1.44)	−25	331	−1.5	−6.1
7	DPA-L	$(CH_2)_2$	100	95	29 100 (1.66)	−15	328	−8.9	−33.4
8	DPA-L	$(CH_2)_3$	97	95	27 200 (1.65)	−33	333	−9.0	−35.1
9	DPA-L	$(CH_2)_4$	100	95	60 600 (1.66)	−32	334	−8.5	−34.3
10	DPA-L	$(CH_2)_5$	98	97	48 500 (1.69)	−35	335	−7.9	−33.0
11	DPA-L	$(CH_2)_6$	100	99	23 300 (1.99)	−27	338	−7.7	−33.2
12	DPA-L	1,4-$CH_2C_6H_4CH_2$	98	97	20 000 (1.46)	−20	318	−6.6	−29.8
13	DPA-F	$(CH_2)_2$	100	96	54 900 (1.63)	−6	322	−10.7	−43.8
14	DPA-F	$(CH_2)_4$	100	96	58 300 (1.72)	−26	349	−10.1	−44.2
15	DPA-F	$(CH_2)_4$	100	96	58 300 (1.72)	−26	349	−10.1	−44.2
16	DPA-F	$(CH_2)_5$	100	96	75 700 (1.81)	−29	348	−9.8	−44.3
17	DPA-F	$(CH_2)_6$	98	96	46 100 (1.63)	−33	359	−9.2	−42.8
18	DPA-F	1,4-$CH_2C_6H_4CH_2$	97	94	27 800 (1.57)	−26	332	−7.0	−34.0

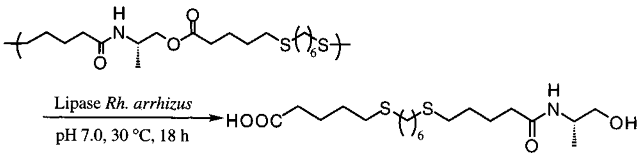
[a] Conditions: concentration of the diolefin and dithiol, 4 M; solvent, DMF; initiator, AIBN 3 mol %; 60 °C; 20 h. [b] Determined by ^1H NMR. [c] Ether-insoluble part. [d] Estimated by GPC based on polystyrene standards; eluent, LiBr solution in DMF (5.8 mM). [e] Determined by DSC. [f] Determined by TGA under nitrogen. [g] Measured by a polarimeter at 26 °C ($c = 1.00$, DMF). [h] Calculated by $[M]_D = [\alpha]_D(M_w$ per unit)/100.

Table 4. Oxidation of Poly(DPA-A-HDG)[a]

			unit ratio[b] (mol %)						
run	oxidant (equiv per S)	time (h)	>S	>S=O	O=(S<)=O	$\bar{M}_n$ $(\bar{M}_w/\bar{M}_n)$[c]	T_g[d] (°C)	T_{d10}[e] (°C)	$[\alpha]_D$[f] (deg)
1	none		100	0	0	48 600 (1.58)	−27	353	−13.6
2	H_2O_2 (1.0)	6	57	43	0	66 500 (1.64)	−25	243	−3.9
3	H_2O_2 (1.0)	9	33	67	0	67 000 (1.61)	−24		−3.3
4	H_2O_2 (1.0)	12	41	59	0	66 000 (1.61)	−23		−3.7
5	H_2O_2 (1.0)	24	42	58	0				
6	H_2O_2 (1.5)	6	16	83	1				
7	H_2O_2 (1.5)	12	5	91	4	61 400 (1.56)	−21		−3.7
8	H_2O_2 (1.5)	24	2	96	2	58 100 (1.51)	−18	238	
9	H_2O_2 (20.0)	24	0	0	100	16 700 (1.20)[h]	16		
10[g]	*m*-CPBA (2.6)	24	0	0	100	14 300 (1.18)[h]	17	314	

[a] Conditions: concentration of poly(DPA-A-HDT), 0.1 M; solvent, $H_2O-CH_2Cl_2 = 1:1$, 25 °C. [b] Determined by ^1H NMR. [c] Estimated by GPC based on polystyrene standards; eluent, LiBr solution in DMF (5.8 mM). [d] Determined by DSC. [e] Determined by TGA under nitrogen. [f] Measured by a polarimeter at 26 °C ($c = 1.00$, DMF). [g] Conditions: concentration of poly(DPA-A-HDT), 0.1 M; solvent, CH_2Cl_2; 25 °C. [h] DMF-soluble and -insoluble parts were obtained.

Scheme 6



polymers. The α-methylene proton of the sulfide group was observed at 2.48−2.60 ppm (top spectrum). Those of sulfoxide and sulfone were observed at 2.60−2.80 ppm (middle spectrum) and 3.00−3.16 ppm (bottom spectrum), respectively. Figure 1B illustrates the IR spectra of the polymers. The characteristic absorption peaks based on sulfoxide and sulfone groups were observed at 1073 and 1285, 1123 cm^{-1}, respectively. The $\bar{M}_n$ of the polymer oxidized to the sulfoxide structure was higher than that before oxidation, while the opposite was for oxidation to the sulfone structure. The increase of the $\bar{M}_n$ from sulfide to sulfoxide may be explained by the molecular weight increase due to the incorporation of oxygen. The lower $\bar{M}_n$ of the polymer oxidized to the sulfone structure may be due to the incomplete solubility of the polymer in DMF. Since no change was observed other than the sulfide unit in the model compound (DPA-F-BT) after oxidation to sulfone with H_2O_2, no polymer chain was cleaved during the oxidation.

Table 5. Enzymatic Degradation of Poly(DPA-A-DT) with Lipase *Rh. arrhizus*[a]

	TOC (ppm)		degradation (%)[b]	
polymer	lipase	non	lipase	non
poly(DPA-A-EDT)	2011	68	16.6	0.6
poly(DPA-A-PrDT)	2924	42	28.3	0.4
poly(DPA-A-BDT)	3129	34	28.6	0.3
poly(DPA-A-PeDT)	3279	78	31.5	0.7
poly(DPA-A-HDT)	1093	42	11.0	0.4

[a] Conditions: lipase *Rh. arrhizus*, 175 unit; 30 °C; 18 h; potassium phosphate buffer (0.2 M) (pH 7.0); enzymatic control (TOC_e), 18 ppm. [b] Percentage degradation = $(TOC - TOC_e)/TOC_{all}100$ (%), = concentration of polymer in buffer (mg/L)(weight of carbon/unit)/(M_w/unit).

Enzymatic degradation of the poly(DPA-A-HDT) film was examined with lipase *Rh. arrhizus* at 30 °C in a pH 7.0 phosphate buffer (Figure 2). It was confirmed that poly(DPA-A-HDT) was gradually degraded enzymatically. The presence of a hydroxy carboxylic acid was confirmed in the buffer solution after degradation for 18 h. It was found that the enzymatic degradation proceeded by hydrolysis of the ester group, as illustrated in Scheme 6.

Table 5 summarizes the enzymatic degradation of the polymers obtained by the polyadditions of DPA-A with dithiols having a several methylene chain length, which was evaluated by the concentration of the total organic

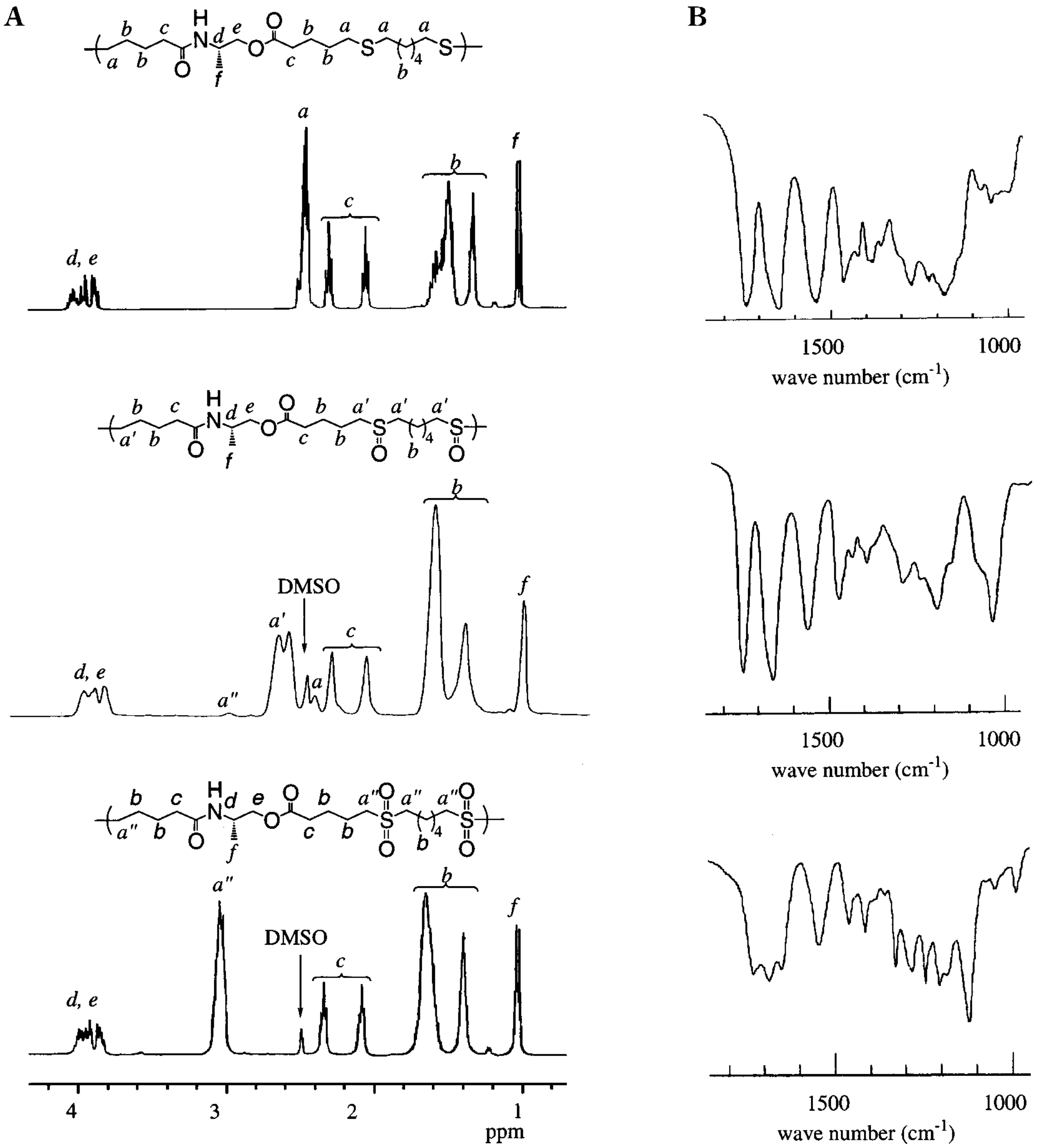


Figure 1. (A) ^{1}H NMR of poly(DPA-A-HDT) (top spectrum) and the polymers oxidized to sulfoxide (middle spectrum) and sulfone (bottom spectrum) structures. The sulfoxide and the sulfone polymers were obtained by oxidations with 1.5 equiv and 20 equiv of H_2O_2 per S group, respectively. (B) IR spectra of poly(DPA-A-HDT) (top spectrum) and the polymers oxidized to sulfoxide (middle spectrum) and sulfone (bottom spectrum) structures.

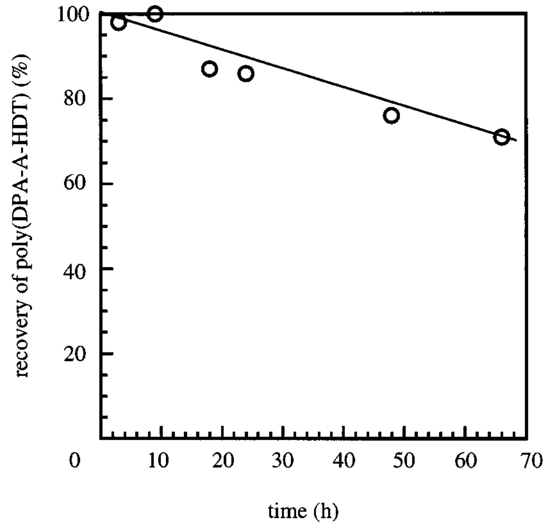


Figure 2. Enzymatic degradation of poly(DPA-A-HDT) film. Recovery of poly(DPA-A-HDT) (%) = weight of the polymer film after degradation/weight of that before degradation.

carbon (TOC) dissolved in the buffer solution. It was found that these polymers were degraded 11.0–31.5% with lipase *Rh. arrhizus*. The percentage degradation value increased as the methylene chain length of the dithiol unit increased, except for poly(DPA-A-HDT). In general, it is known that biodegradability of synthetic polymers is affected by the flexibility and the hydrophobic–hydrophilic balance of the polymers. For example, it has been reported that aliphatic polyesters having six and eight methylene chains show larger degradability with *Aspergillus niger* than those having two, four, ten, and twelve methylene chains.[9]

Summary

In this paper, novel enzymatically degradable poly(ester-amide-sulfide)s, based on optically active amino alcohols, could be synthesized by the radical polyadditions of dithiols with diolefins derived from optically active amino alcohols in high yields. The poly(ester-amide-sulfoxide)s and poly(ester-amide-sulfone)s could be selectively obtained by the oxidation of the poly(ester-amide-sulfide)s with 1.5 and 20 equiv of hydrogen peroxide, respectively. No polymer chain was cleaved during the oxidation. The poly(ester-amide-sulfide)s were degraded with lipase *Rh. arrhizus* to afford a hydroxy carboxylic acid, which was formed by the hydrolysis of the ester group.

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Supporting Information Available: Analytical data for diolefins (DPA-L and DPA-F), adducts of DPA-F with thiols (DPA-F-PrT, DPA-F-BT, DPA-F-PeT, DPA-F-HT, and DPA-F-BzlT), polymers poly(DPA-A-PrDT), poly(DPA-A-BDT), poly(DPA-A-PeDT), poly(DPA-A-HDT), poly(DPA-A-XDT), poly(DPA-L-EDT), poly(DPA-L-PrDT), poly(DPA-L-BDT), poly(DPA-L-PeDT), poly(DPA-L-HDT), poly(DPA-L-XDT), poly(DPA-F-EDT), poly(DPA-F−PrDT), poly(DPA-F−BDT), poly(DPA-F−PeDT), poly(DPA-F−HDT), and poly(DPA-F-XDT)). Figure S1 of the ^{1}H NMR spectrum of DPA-A (solvent: $CDCl_3$, 90 MHz) and Figure S2 of the ^{1}H NMR spectrum of DPA-F-ET (solvent: $CDCl_3$, 400 MHz). Ordering and internet accessing information for these 11 pages is given on any current masthead page.

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(8) All compounds showed a positive bimodal Cotton effect in the CD spectra (1×10^{-5} M, tetrahydrofuran). Wavelengths of the peak tops and molecular ellipticities for the Cotton effect of poly(DPA-F-EDT), poly(DPA-F-PeDT), poly(DPA-F-HDT) and model compounds of the polymers, DPA-F-ET, DPA-F-PeT, and DPA-F-HT, were 213, 214, 214, 214, 215, 215 nm and 23 926, 12 985, 12 943, 10 620, 12 790, and 12 903 (deg·cm^2)/dmol, respectively.

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