gration against the mesitylene standard.

Chain Transfer Using W(CHPh)(NAr)(O-*t*-Bu)$_2$. W(CH-*t*-Bu)(NAr)(O-*t*-Bu)$_2$ (20 mg, 0.035 mmol) was dissolved in ~1 mL of C_6D_6 containing 9 mg of mesitylene as an NMR standard. This solution was treated with 34 mg of norbornene (0.361 mmol, 10 equiv) in ~1 mL of C_6D_6. The solution was then split into two and one portion was treated with 12 mg of 1-(2-cyclopentenylmethyl)-2-phenylethene (0.065 mmol, 3.7 equiv) in C_6D_6. The alkylidene H_α resonance for the living polymer disappeared and that characteristic of the benzylidene proton in W(CHPh)(NAr)(O-*t*-Bu)$_2$ appeared in ~60% yield over a period of ~1 h.

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Registry No. **1a**, 107440-84-6; **1b**, 120173-01-5; **1c**, 112481-72-8; **1d**, 120204-18-4; **1e**, 120173-02-6; **2a**, 120172-98-7; **2b**, 120172-95-4; **2c**, 120172-96-5; **2d**, 120173-00-4; **3a**, 120172-99-8; **3c**, 20837-03-0; **4a**, 13705-23-2; **4c**, 824-90-8; **4e**, 116269-95-5; **5**, 120172-97-6; cyclopentene (homopolymer), 25103-85-9; polypentenamer, 28702-43-4; norbornene (homopolymer), 25038-76-0.

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Poly(anhydrides). 3. Poly(anhydrides) Based on Aliphatic–Aromatic Diacids

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ABSTRACT: Poly(anhydrides) containing aliphatic and aromatic moieties, poly(ω-(*p*-carboxyphenoxy)alkanoic anhydride), of the structure $-(COC_6H_4O(CH_2)_xCOO)_n-$ (x = 1, 4, and 7) were synthesized by either melt or solution polymerization with molecular weights of up to 44 600. These polymers displayed a zero-order hydrolytic degradation profile for 2–10 weeks. The longer the length of the alkanoic chain, the longer the degradation rate. Stability studies under anhydrous conditions showed that these polymers were stable in solid state for over 6 months at 25 °C but underwent reversible self-depolymerization in chloroform solution.

Introduction

The surface-eroding properties of poly(anhydrides) (PA) in aqueous medium makes them desirable for controlled release of therapeutic substances.[1-3] These PA degrade by hydrolysis into nontoxic acid derivatives and show favorable biocompatibility in tissue response and toxicological studies.[3] The hydrolytic degradation rates can be altered several thousand-fold by simple changes in the polymer backbone.[1] Aliphatic poly(anhydrides) degrade in a few days while some aromatic poly(anhydrides) degrade over a period of few years.[2] Aromatic polyanhydrides display a zero-order degradation profile.[2] These aromatic polymers have low solubility in common organic solvents and have high melting points; therefore they cannot be easily fabricated into either microspheres or films. The degradation rates of copolymers made of aliphatic and aromatic moieties vary between these extremes, depending on the aromatic content.[1-4] However, in such copolymers the aliphatic regions degrade faster, and thus the aromatic component content of the device increases for a long period of time,[5] leading to a lack of linearity in the degradation process. We now report on new poly(anhydrides) that display zero-order degradation profiles over variable periods of time (i.e., days to months). These polymers are soluble in common organic solvents and have low melting points.

In contrast to copolymers based on aliphatic and aromatic diacids, these new homopoly(anhydrides) have the aliphatic and aromatic moieties combined into one identity. These monomers can be viewed as containing an aromatic head and an aliphatic tail. The addition of a monomer to the growing polymeric chain could result in a head-to-head (i.e., aromatic–aromatic), head-to-tail, or tail-to-tail sequence. Consequently, these polymers are

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characterized by a uniform distribution of aliphatic and aromatic residues in the polymeric chain. This uniformity is advantageous over copolymers of aromatic and aliphatic diacids which are characterized by a random chain structure of aliphatic and aromatic blocks.[4,5] Hence, we have proposed that the aliphatic–aromatic homopolymers will display uniform hydrolytic degradation profile (zero order in slabs). Additionally, we have studied these polymers in solid state and in solution to examine their stability.

Experimental Section

Materials. Diphosgene (Thiokol), methyl *p*-hydroxybenzoate, methyl *m*-hydroxybenzoate, methyl bromoacetate, methyl 3-bromopropionate, methyl 5-bromovalerate, 8-bromooctanoic acid, *p*-nitroaniline, poly(4-vinylpyridine), and triethylamine were all from Aldrich, Milwaukee, WI. Anhydrous chloroform (Aldrich, water <0.005%) for stability studies was dried over activated alumina and freshly distilled under nitrogen before use.

Instrumentation. Infrared spectroscopy was performed on a Perkin-Elmer 1430 spectrophotometer (Perkin-Elmer, MA). Polymeric samples were film cast onto NaCl plates from a solution of the polymer in chloroform. Prepolymer samples were either pressed into KBr pellets or dispersed in Nujol onto NaCl plates. The melting points of prepolymers were determined on a Fisher Johns melting point apparatus. The molecular weights of the polymers and prepolymers were estimated on a Perkin-Elmer GPC system (Perkin-Elmer, MA) consisting of a Series 10 pump and a 3600 data station with a LKB 214 rapid spectral detector at 254-nm wavelength. Samples were eluted in chloroform through two PL gel columns (Polymer Laboratories; 100- and 1000-α pore sizes) in series at a flow rate of 1.5 mL/min. Molecular weights of polymers were determined relative to poly(styrene) standards (Polysciences, PA, molecular weights range 500–160 000) by using CHROM 2 and GPC 4 computer programs (Perkin-Elmer, MA). Elemental analysis was performed by Galbraith Laboratories (Knoxville, TN). ^{1}H NMR spectra were obtained on a Varian 250-MHz spectrophotometer, using deuterated chloroform as a solvent and tetramethylsilane (TMS) as an internal reference. When acids were analyzed, samples were dissolved in a 0.1 N solution of K_2CO_3 in D_2O, and TMS was used as an external reference. UV measurements were performed on a Perkin-Elmer 553 UV–vis spectrophotometer.

Methyl 8-Bromooctanoate. Methyl 8-bromooctanoate was prepared by using the method of Greenstein.[6] To chilled methanol (150 mL, at −40 °C), thionyl chloride (27.8 g, 0.23 mol) was added dropwise over a few minutes with vigorous stirring. To this mixture, 8-bromooctanoic acid (44. g, 0.20 mol) was added, and the resulting mixture was stirred at 25 °C for 3 h at 37 °C overnight. The clear colorless solution was evaporated in vacuo to give 36 g (78%) of a slightly yellow oil; IR 1740 cm^{-1} (ester).

Preparation of ω-(*p*-Carboxyphenoxy)alkanoic Acids. The ω-(*p*-carboxyphenoxy)alkanoic acids were hydrolyzed from the corresponding dimethyl esters. These dimethyl esters were prepared by the modified literature procedure.[7] As an example, 5-(*p*-carboxyphenoxy)valeric acid dimethyl ester (CPV diester) was prepared as follows. Freshly cut sodium metal (5.98 g, 0.26 mol) was gradually introduced into dry methanol (150 mL) in a 1000-mL round-bottomed flask equipped with a stirrer and a reflux condenser with a drying tube. Upon completion, methyl *p*-hydroxybenzoate (39.56 g, 0.26 mol) in methanol (100 mL) followed by methyl 5-bromovalarate (50.0 g, 0.26 mol) was added rapidly. After 78 h, the precipitate was filtered, and the white diester precipitated upon pouring the solution into ice water. The precipitate was dried overnight and weighed (58.35 g, 84%). ^{1}H NMR ($CDCl_3$) δ 7.98 (d, 2, J = 5 Hz), 6.88 (d, 2, J = 5 Hz), 4.02 (t, 2, J = 3 Hz), 3.88 (s, 3), 3.68 (s, 3), 2.41 (t, 2, J = 3 Hz), 1.84 (t, 4, J = 2.5 Hz); IR (Nujol) 1740, 1710, 1600 cm^{-1}; mp 43–45 °C.

8-(*p*-Carboxyphenoxy)octanoic acid dimethyl ester (CPO diester) was prepared similarly by using methyl 8-bromooctanoate (75%). ^{1}H NMR ($CDCl_3$) δ 7.00 (d, 2, J = 9 Hz), 4.00 (d, 2, J = 6 Hz), 2.25 (t, 2, J = 7 Hz), 1.17 (t, 2, J = 6 Hz), 1.52 (t, 4, J = 7 Hz), 1.31 (s, 6); IR (Nujol) 1730, 1710, 1600 cm^{-1}; mp 57–58 °C.

2-(*p*-Carboxyphenoxy)acetic acid dimethyl ester (CPA diester) was prepared similarly by using methyl bromoacetate (85%). ^{1}H NMR ($CDCl_3$) δ 8.00 (d, 2, J = 9 Hz), 6.92 (d, 2, J = 8 Hz), 4.70 (s, 2), 3.89 (s, 3), 3.82 (s, 3); IR (Nujol) 1770, 1710, 1600 cm^{-1}; mp 94–95 °C.

4-(*m*-Carboxyphenoxy)valeric acid dimethyl ester (*m*-CPV diester) was prepared similarly by using methyl *m*-hydroxybenzoate and methyl 5-bromovalerate (65%). ^{1}H NMR ($CDCl_3$) δ 7.63 (d, 1, J = 9 Hz), 7.54 (t, 1, J = 2 Hz), 7.08 (d, 1, J = 5 Hz), 4.02 (t, 2, J = 2.5 Hz), 3.91 (s, 3), 3.68 (s, 3), 2.41 (t, 2, J = 3 Hz), 1.84 (t, 4, J = 2.5 Hz); IR (Nujol) 1750, 1730, 1590 cm^{-1}; mp 39–42 °C.

The above dimethyl esters were hydrolyzed to the corresponding diacids. A solution of NaOH (2 N, 600 mL) was added to the diester in a 1000-mL round-bottomed flask equipped with a condenser and a mechanical stirrer. The solution was allowed to reflux for 10 h with stirring. After the solution was cooled to 30 °C it was acidified by adding concentrated sulfuric acid. The precipitate was filtered from solution, washed with water and allowed to dry overnight.

5-(*p*-Carboxyphenoxy)valeric acid (CPV) was prepared by the hydrolysis of the CPV diester to yield 57.00 g (93%). ^{1}H NMR (D_2O, K_2CO_3) δ 7.80 (d, 2, J = 8 Hz), 6.91 (d, 2, J = 8 Hz), 3.95 (d, 2, J = 6 Hz), 2.19 (t, 2, J = 6 Hz), 1.66 (m, 4); IR (Nujol) 1690, 1600 cm^{-1}; mp 195–198 °C.

8-(*p*-Carboxyphenoxy)octanoic acid (CPO) was prepared by the hydrolysis of the CPO diester (90%). ^{1}H NMR (D_2O, K_2CO_3) δ 7.845 (d, 2, J = 9 Hz), 6.98 (d, 2, J = 9 Hz), 4.03 (t, 2, J = 6 Hz), 2.16 (t, 2, J = 6 Hz), 1.72 (t, 2, J = 6 Hz), 1.53 (t, 2, J = 7 Hz), 1.31 (m, 6); IR (Nujol) 1690, 1680, 1600 cm^{-1}; mp 204–206 °C.

2-(*p*-Carboxyphenoxy)acetic acid (CPA) was prepared by the hydrolysis of the CPA diester (91%). ^{1}H NMR (D_2O, K_2CO_3) δ 7.89 (d, 2, J = 9 Hz), 6.96 (d, 2, J = 9 Hz), 4.54 (s, 2 H); IR (Nujol) 1730, 1710, 1600 cm^{-1}; mp 158–160 °C.

5-(*m*-Carboxyphenoxy)valeric acid (*m*-CPV) was prepared by the hydrolysis of the *m*-CPV diester (90%). ^{1}H NMR (D_2O, K_2CO_3) δ 6.82 (m, 3), 6.55 (d, 1, J = 5 Hz), 3.55 (t, 2, J = 6 Hz), 1.67 (t, 2, J = 7 Hz), 1.22 (m, 4); IR (Nujol) 1700, 1680, 1580 cm^{-1}; mp 185–187 °C.

Prepolymer Synthesis. 5-(*p*-Carboxyphenoxy)valeric acid prepolymer (CPV prepolymer) was prepared as follows: a solution of CPV (57.00 g) in acetic anhydride (600 mL) in a 1000-mL round-bottomed flask equipped with a condenser and a stirrer was heated at reflux for 6 h with stirring. The reaction mixture was evaporated to dryness. A diethyl ether–hexane mixture was added to the solid to extract any acetic anhydride residues, and the resulting mixture was swirled overnight. After decanting, petroleum ether (100 mL) was added to the solution, and the prepolymer was filtered and dried to yield 50 g (60%) of prepolymer. ^{1}H NMR ($CDCl_3$) δ 8.00 (d, 2, J = 7 Hz), 6.94 (d, 2, J = 9 Hz), 4.06 (t, 2, J = 6 Hz), 2.57 (t, 2, J = 6 Hz), 2.22 (s, 6), 1.89 (m, 4); IR (Nujol) 1820, 1740, 1600 cm^{-1}; mp 54–55 °C; number-average molecular weight (M_n) 187; weight-average molecular weight (M_w) 195 (both M_n and M_w were determined by GPC).

8-(*p*-Carboxyphenoxy)octanoic acid prepolymer (CPO prepolymer) was prepared similarly from CPO diacid (65%). ^{1}H NMR ($CDCl_3$) δ 8.01 (d, 2, J = 9 Hz), 6.96 (d, 2, J = 9 Hz), 4.03 (t, 2, J = 6 Hz), 2.60 (t, 2, J = 6 Hz), 2.15 (s, 3), 1.82 (m, 4), 1.40 (m, 6). IR (Nujol) 1800, 1730, 1600 cm^{-1}; mp 59–60 °C; M_n 118; M_w 132.

2-(*p*-Carboxyphenoxy)acetic acid prepolymer (CPA prepolymer) was prepared similarly from CPA diacid (70%). ^{1}H NMR ($CDCl_3$) δ 8.05 (m, 2); 7.01 (t, 2, J = 4 Hz), 5.50 (s, 2), 2.155 (s, 6); IR (Nujol) 1820, 1790, 1730, 1600 cm^{-1}; mp 61–62 °C; M_n 231; M_w 995.

5-(*m*-Carboxyphenoxy)valeric acid prepolymer (*m*-CPV prepolymer) was prepared similarly from *m*-CPV diacid (52%). ^{1}H NMR ($CDCl_3$) δ 7.65 (d, 1, J = 5 Hz), 7.55 (m, 1), 7.37 (t, 1, J = 3.5 Hz), 7.18 (d, 1, J = 5 Hz), 4.03 (m, 2), 2.57 (m, 2), 2.38 (s, 2), 2.17 (s, 5), 1.88 (m, 4); IR (Nujol) 1810, 1740, 1600, 1580 cm^{-1}; mp <30 °C; M_n 449; M_w 472.

Polymer Synthesis. Poly(ω-(*p*-carboxyphenoxy)alkanoic anhydrides) were synthesized by either melt–polycondensation or by solution polymerization.

Melt Polycondensation. The diacid monomers were converted into the mixed anhydride of acetic acid and polymerized as previously described.[4] In a typical reaction, CPV prepolymer

Scheme I

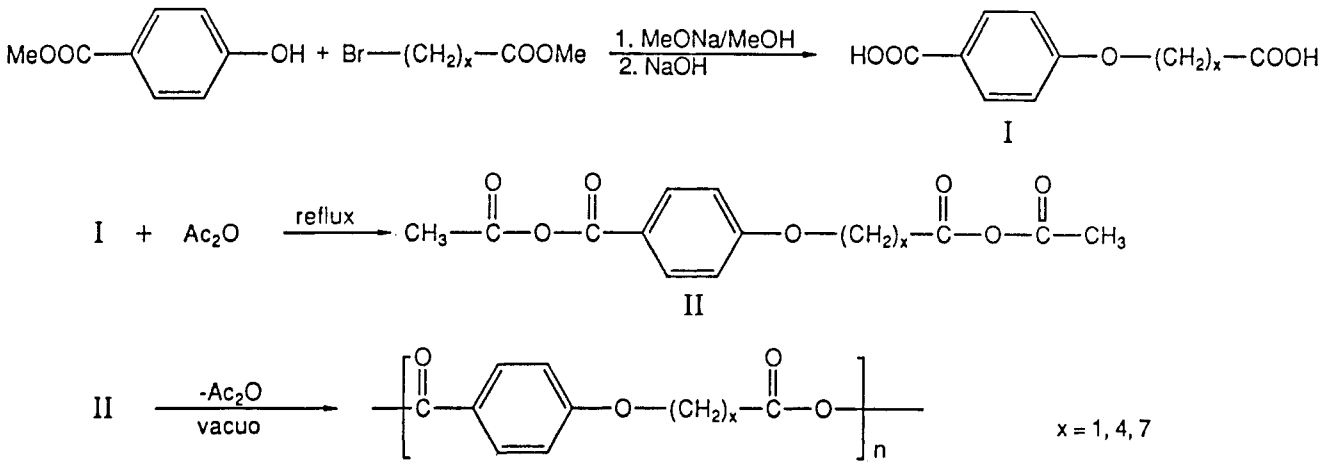

Table I
Melt Polymerization of Poly(ω-(*p*-carboxyphenoxy)alkanoic anhydride)[a]

polymer	mol wt[b] M_w	mol wt[b] M_n	$[\eta]$, dL/g	mp, °C	IR,[c] cm^{-1}
poly(CPA)				204–205	1720, 1770, 1795
poly(CPV)	44600	18950	0.58	50–51	1720, 1770, 1795
poly(CPO)	33300	15300	0.46	53–54	1720, 1780, 1800
poly(CPV–CPO)	24600	9400	0.37	40–43	1720, 1780, 1800
poly(CPA–CPV)	21800	10100	0.32	62–65	1720, 1780, 1800
poly(CPA–CPO)	20850	9850	0.31	58–60	1720, 1780, 1800
poly(*m*-CPV)	13630	5640	0.30	37–40	1740, 1780, 1810

[a] Polymerized by melt polycondensation at 180 °C. [b] M_w and M_n were determined by GPC (see Experimental Section). [c] Characteristic absorbancies of the anhydride bonds. [d] CPA, CPV, and CPO are ω-(*p*-carboxyphenoxy)acetic, -valeric, and -octanoic acid, respectively. *m*-CPV is 4-(*m*-carboxyphenoxy)valeric acid.

(2.0 g) was placed in a Kimax glass tube (20 × 2 cm) with a side arm equipped with a nitrogen inlet. The tube was immersed in an oil bath at 180 °C. After the prepolymer was melted (1 min), high vacuum (0.01 mmHg) was applied through the side arm. The condensation product (acetic anhydride) was trapped in a dry ice/acetone trap. During the polymerization, a strong nitrogen sweep with vigorous agitation of the melt was performed for 30 s every 15 min. The crude polymer was purified by precipitating it in dry petroleum ether from a chloroform solution. Melting point, IR data, and molecular weight are shown in Table I. Elemental analysis: poly(CPA) ($C_9H_6O_4$), C, 59.2, O, 35.4, H, 3.1 (calcd C, 60.7, O, 35.9, H, 3.4); poly(CPV) ($C_{12}H_{12}O_4$) C, 63.7, O, 29.5, H, 5.1 (calcd C, 64.5, O, 29.1, H, 5.5); poly(CPO) ($C_{15}H_{18}O_4$) C, 68.2, O, 24.1, H, 6.5 (calcd C, 68.7, O, 24.4, H, 6.9); poly(*m*-CPV) ($C_{12}H_{12}O_4$) C, 63.8, O, 29.5, H, 5.2 (calcd C, 64.5, O, 29.1, H, 5.5).

Solution Polymerization. Polymers were synthesized according to a general procedure previously described.[8] In a typical reaction, CPV was polymerized as follows: diphosgene (0.5 g, 0.5 equiv) was added dropwise into a stirred mixture of 5-(*p*-carboxyphenoxy)valeric acid (2 g, 1.0 equiv) and poly(4-vinylpyridine) (3 g, 2.5 equiv) in chloroform (20 mL). After 3 h at 25 °C the insoluble PVP·HCl was removed by filtration. The filtrate was washed with anhydrous diethyl ether and dried at 40 °C for 24 h in a vacuum oven.

Insoluble poly(anhydride), poly(2-(*p*-carboxyphenoxy)acetic anhydride), was polymerized as above, but triethylamine (TEA), as a soluble acid acceptor, was used instead of the insoluble PVP. The polymer precipitated during the polymerization and was isolated by filtration.

Stability Studies. Stability studies in solid state and in chloroform solution were performed as previously described.[9] Briefly, polymer powder (200 mg) was stored in glass ampules in vacuo immediately after synthesis. Stability in solution was performed in anhydrous chloroform (10 mg/mL) at 37 °C.

The molecular weight was followed by GPC at different time points. The depolymerization products were analyzed by IR and ^1H NMR spectroscopies and were compared to the original polymers. These depolymerization products were repolymerized at 180 °C in vacuo for 30 min.

Hydrolytic Degradation. Disk-shaped samples of 200 mg of polymer, 15 mm in diameter and 1 mm thick, were prepared by compression molding (Carver Press) at 30000 psi. Hydrolytic degradation was performed at 37 °C in a sodium phosphate buffer (0.1 M, pH 7.4). The degradation was followed by measuring the UV absorbance at 235 nm of the periodically changed buffer solution. *p*-Nitroaniline (PNA) powder (particle size <100 μm) was mixed (5% w/w) with the polymer before compression molding. The release of PNA was followed by a UV spectrophotometer at 380 nm.

Table II
Solution Polymerization of ω-(*p*-Carboxyphenoxy)alkanoic Acids[a]

polymer	mol wt[b] M_w	mol wt[b] M_n	mp, °C	yield, %
poly(CPA)			185–187	77
poly(CPV)	12850	6450	50–52	68
poly(CPO)	9400	4490	48–51	75
poly(CPV–CPO)	10250	4810	45–48	72
poly(CPA–CPV)	9150	4900	40–43	67
poly(CPA–CPO)	11210	5010	44–46	81

[a] Polymerization in chloroform solution at 25 °C using poly(4-vinylpyridine) as an acid acceptor and diphosgene as a coupling agent. [b] M_w and M_n were determined by GPC (see Experimental Section).

Results and Discussion

Polymers of ω-(carboxyphenoxy)alkanoic acid of 1, 4, and 7 methylene groups were synthesized by melt polycondensation (Scheme I). The data analysis of these polymers is summarized in Table I. Polymers of weight-average molecular weight up to 44600 were obtained. Poly(CPV) and poly(CPO) were similar in appearance and physical properties. Both were pliable, soluble in common organic solvents, had film-forming (solvent cast) properties, and low melting points. Poly(CPA) was a brittle polymer with a high melting point (204–5 °C). Copolymerization of CPA with either CPV or CPO yielded a soluble polymer with similar physical properties to poly(CPV) (Table I).

Solution Polymerization. Polymers were synthesized by using diphosgene as a coupling agent and poly(4-vinylpyridine) as an insoluble acid acceptor. This method was previously reported to yield highly pure polymers.[8] The data for the solution polymerization of ω-(*p*-carboxyphenoxy)alkanoic acids are summarized in Table II. Polymers with weight-average molecular weight up to

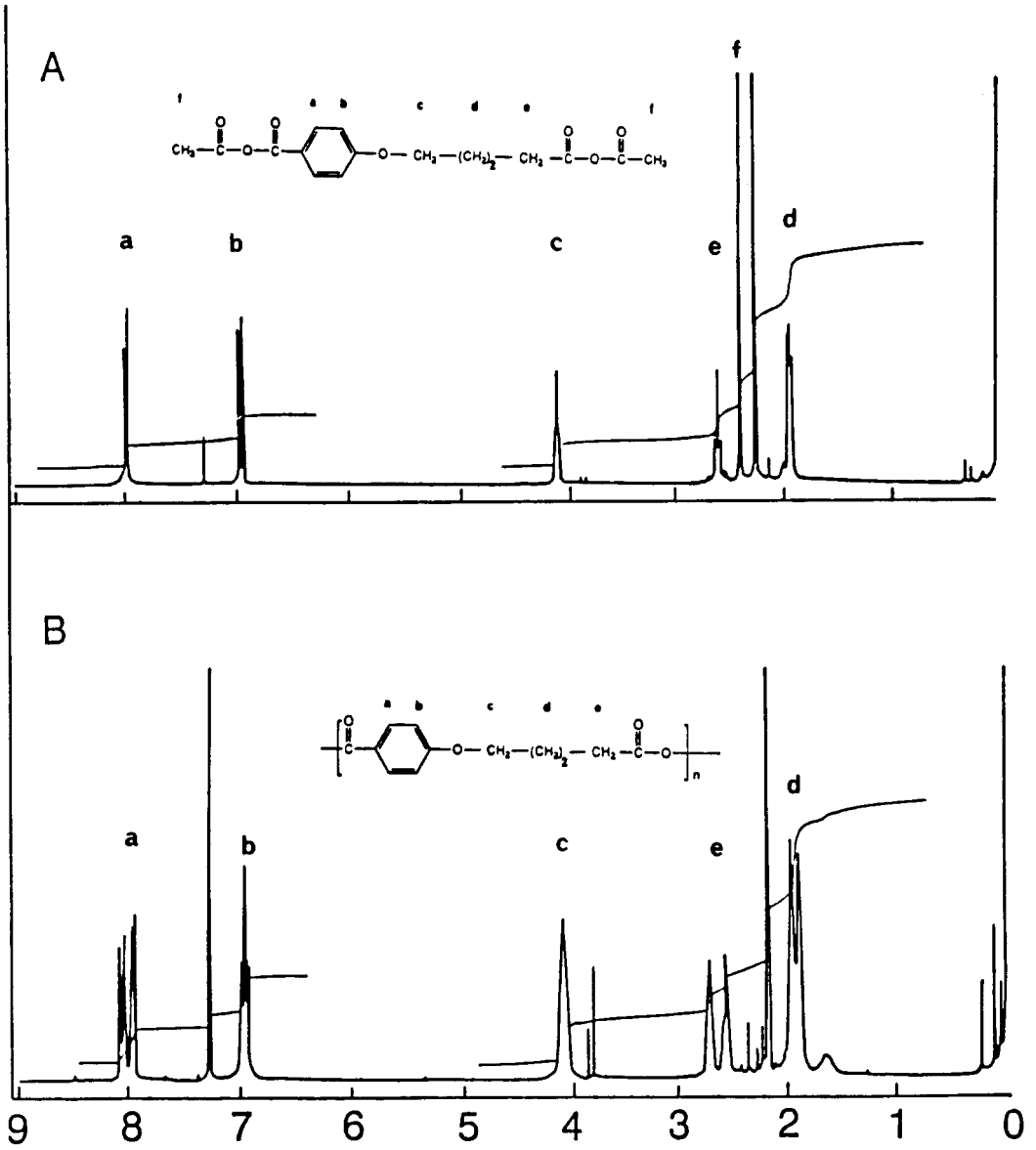

Figure 1. ^{1}H NMR spectra (in ppm) of (A) CPV prepolymer and (B) poly(CPV).

12 850 were obtained. The polymers showed ^{1}H NMR and IR spectra and melting points similar to the corresponding polymers prepared by the melt polymerization.

Polymer Characterization. The aliphatic–aromatic diacids can be connected by an anhydride bond in the polymer by (1) an aliphatic moiety and an aliphatic moiety (tail-to-tail), (2) an aliphatic moiety and an aromatic moiety (tail-to-head or head-to-tail), or (3) an aromatic moiety and an aromatic moiety (head-to-head). These three possibilities are reflected in the IR and ^{1}H NMR spectra. The IR spectrum of poly(CPV) showed a characteristic anhydride carbonyl stretching at 1720, 1780, and 1800 cm^{-1} (aliphatic anhydrides 1720, 1800 cm^{-1}, and conjugated noncyclic anhydrides at 1720 and 1780 cm^{-1}). The distribution of the three types of anhydride bonds in the polymer was determined by ^{1}H NMR spectroscopy. The ^{1}H NMR spectra of the CPV prepolymer and polymer are shown in Figure 1. The methylenic protons of the aliphatic residue conjugated to the anhydride bond appeared as two triplets, at 2.54 ppm (J = 3 Hz) and at 2.72 ppm (J = 3 Hz). The aromatic protons ortho to the anhydride bond appeared in two chemical shifts, a doublet at 7.90 ppm (J = 8 Hz), and a doublet at 8.10 ppm (J = 8 Hz). The peaks at 2.72 and 8.10 ppm are not observed in the ^{1}H NMR spectrum of the prepolymers (Figure 1). These peaks were explained by a chemical shift effect across the anhydride bond, affecting the ^{1}H NMR absorbancies of the α-protons connected to the anhydride bond. These peaks were attributed to the three types of anhydride bonds in the polymer: (1) the triplet at 2.54 ppm is of aliphatic–aliphatic anhydride bond (tail-to-tail), (2) the triplet at 2.72 ppm is of aliphatic–aromatic (head-to-tail) and the doublet at 7.90 ppm is of aromatic–aliphatic (head-to-tail), and (3) the doublet at 8.10 ppm is of aromatic–aromatic anhydride bond (head-to-head). A careful examination of the integration of these peaks revealed a ratio of 1:2:1, tail-to-tail, tail-to-head and head-to-tail, and head-to-tail, respectively. Identical results were found for all the other aromatic–aliphatic poly(anhydrides). This ratio implies an equal statistical distribution of alternating head-to-head and tail-to-tail units throughout the polymer backbone.

Stability in Solid State and Chloroform Solution. Poly(CPV) and poly(CPO) in solid state (M_w 44 600 and 33 300, respectively) were stored in vacuo at 25 °C, and the molecular weight was monitored as a function of time. After 6 months of storage, both polymers were still pliable, and no decrease in molecular weight was observed. The

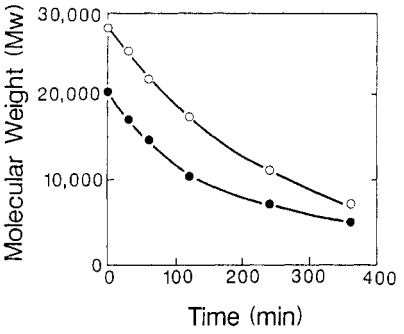

Figure 2. Depolymerization of poly(CPO) (○) and poly(CPV) (●) in solution. Polymer in chloroform (10 mg/mL) depolymerized at 37 °C.

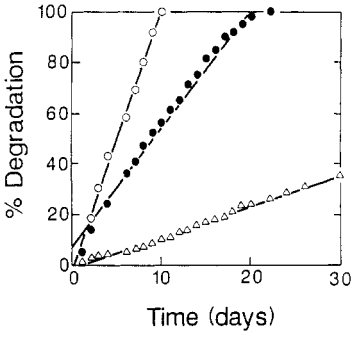

Figure 3. Degradation of poly(ω-(*p*-carboxyphenoxy)alkanoic anhydrides). Disks (15 × 1 mm) in phosphate buffer (pH 7.40) at 37 °C: ○, poly(CPA); ●, poly(CPV); △, poly(CPO).

polymers were more stable than aliphatic PA, which showed a significant decrease in molecular weight with time.[9] The stability of the polymers in chloroform solution is described in Figure 2. A significant decrease in molecular weight was observed for both polymers. The decrease in molecular weight was not effected by traces of water.[9] Using methodology that was previously established,[9] repolymerization of the depolymerization products (M_w = 5200 and 7350 for poly(CPV) and poly(CPO), respectively) yielded polymers with the original high weight-average molecular weight (17 900 and 28 450, respectively). The decrease in molecular weight was a self-depolymerization process as revealed from the similarity between the depolymerization products and the original polymers (determined by IR and ^{1}H NMR spectroscopies) and the reversibility of the depolymerization process.[9]

Hydrolytic Degradation. The hydrolytic degradation of aromatic–aliphatic homopolymers is described in Figure 3. The polymers display a zero-order degradation profile. The degradation rate is dependent on the length of the alkanoic acid residue in the diacid monomer, i.e., slower degrdn. rates were observed for diacids with longer alkanoic residues. The release properties of these polymers were examined by the release of PNA from poly(CPV) in vitro in a sodium phosphate buffer (0.1 M, pH 7.4; Figure 4). PNA was chosen as a model drug because of its UV absorbance spectrum, which allows the simultaneous determination of degradation products and drug release. The release of PNA followed the degradation of the polymer. This profile was representative of a uniform degradation and release rate.

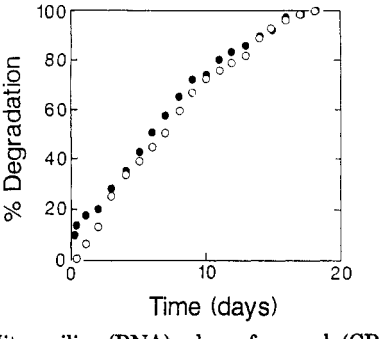

Figure 4. *p*-Nitroaniline (PNA) release from poly(CPV). Release from compression molded disks containing 5% (w/w) PNA, in phosphate buffer (pH 7.40) at 37 °C: ○, degradation; ●, PNA release.

In summary, this study presents the synthesis of a new class of homopoly(anhydrides), based on aliphatic–aromatic diacids, desirable for controlled release applications. These polymers have low melting points, thus they are suitable for hot-melt microencapsulation[10] and injection molding fabrication methods for thermally sensitive drugs. Their solubility in common organic solvents allows solution fabrication techniques. The aliphatic–aromatic polymers display homodistribution of alternating aliphatic and aromatic groups and display a zero-order degradation and release profile in physiological media throughout the whole degradation period.

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Registry No. CPV diester, 35005-33-5; CPO diester, 120333-27-9; CPA diester, 35005-30-2; *m*-CPV diester, 120333-28-0; CPV, 35005-21-1; CPO, 117412-57-4; CPA, 19360-67-9; *m*-CPV, 120333-29-1; CPV (homopolymer), 117381-42-7; CPA (homopolymer), 117412-54-1; *m*-CPV (homopolymer), 120333-30-4; (CPV)(CPO) (copolymer), 120333-31-5; (CPA)(CPV) (copolymer), 120333-32-6; (CPA)(CPO) (copolymer), 120333-33-7; methyl *p*-hydroxybenzoate, 99-73-3; methyl 5-bromovalarate, 5454-83-1; methyl 8-bromooctanoate, 26825-92-3; methyl bromoacetate, 96-32-2; methyl *m*-hydroxybenzoate, 19438-10-9; CPO (homopolymer), 117441-95-9.

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