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Poly(anhydrides). 2. One-Step Polymerization Using Phosgene or Diphosgene as Coupling Agents

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ABSTRACT: Two approaches for one-step solution polymerization of poly(anhydrides) at ambient temperature were developed. In the first approach highly pure polymers (>99.7%) were obtained by the use of sebacoyl chloride, phosgene, or diphosgene as coupling agents and poly(4-vinylpyridine) or K_2CO_3 as insoluble acid acceptors. In this approach, the polymer is exclusively soluble in the reaction solution and the only byproduct formed is the insoluble acid acceptor–hydrochloric acid salt. Polymerization of sebacic acid with phosgene, either as a gas or in solution, or diphosgene as a coupling agent with triethylamine as an acid acceptor yielded a polyanhydride with a weight average molecular weight up to 16300. This poly(anhydride) was contaminated with $Et_3N{\cdot}HCl$ (up to 80%, mol %). The use of insoluble acid acceptors gave pure polymers (>99.7%) with a weight average molecular weight up to 13950. The second approach for one-step synthesis of pure poly(anhydrides) was the use of an appropriate solvent where the polymer is exclusively soluble but the corresponding polymerization byproduct (e.g., $Et_3N{\cdot}HCl$) is insoluble. Under this condition polymerization of sebacic acid gave the best results in *N,N*-dimethylformamide and in toluene.

Introduction

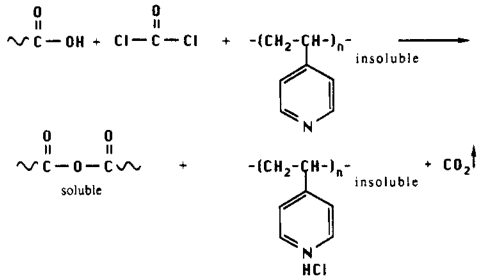
Several studies have shown that poly(anhydrides) have unique properties: they are biodegradable, and display surface erosion, and erosion rates can be changed several thousand-fold by simple changes in the choice of monomer.[1-4] However, approaches for synthesizing highly pure poly(anhydrides) have yet to be developed. In a previous report[5] we described an improved melt–polycondensation method in which poly(anhydrides) were synthesized from highly pure prepolymers under optimized conditions. Although high molecular weight pure polymers were obtained,[5] this method could be applied only to heat-stable monomers. On the other hand, solution polymerization is well-suited for heat-sensitive monomers such as poly(anhydrides) of dipeptides and therapeutically active diacids.

A variety of solution polymerizations of poly(anhydrides) at ambient temperature have been reported.[6-9] Partial hydrolysis of diacid chloride in the presence of pyridine as an acid acceptor yielded very low molecular weight polymers (e.g., for poly(terephthalic anhydride), MW was 2100).[8] The use of dehydration agents may also effect poly(anhydride) formation.[9] The use of *N,N*-bis(2-oxo-3-oxazolidinyl)phosphoramido chloride, dicyclohexylcarbodiimide, and chlorosulfonyl isocyanate as coupling agents have been reported.[9] These coupling agents yielded impure polymers of low molecular weight. In all previously reported methods the final products contained polymerization byproducts (e.g., amine–hydrochloride, dehydration agents residues) which had to be removed by washing with protic solvents. This last purification step may cause hydrolysis of the polymer (vide infra). In addition, the need for diacid chloride prepolymers of high purity requires an additional synthetic step.

Dichloroformate (phosgene) is a reactive gas that is commonly used in organic synthesis.[10] Yet, its vapor toxicity limits its applicability. Trichloromethyl chloroformate (diphosgene) is a phosgene dimer and can be viewed as a liquid phosgene substitute.[11] The use of diphosgene has advantages over phosgene:[11] (1) it is a liquid with low vapor pressure at room temperature, (2) reactions are simpler to perform as no elaborate traps are needed, and (3) it can be weighed directly. Diphosgene has been used for various applications in organic synthesis. Alcohols react with diphosgene to give the corresponding carbonate or in the presence of amine base (e.g., pyridine) the chloroformate.[12] Isocyanates and ureas are prepared from the reaction of diphosgene and amine. *N*-Carboxy-α-amino acid anhydrides were prepared by the reaction of α-amino acids with either phosgene or diphosgene.[13] The use of phosgene in poly(anhydride) synthesis has been previously attempted;[14] however, only sebacic acid oligomers were obtained (DP = 7).

In searching for an alternative synthetic method, we sought an approach where sensitive diacids could be converted to the corresponding polymer, at ambient temperature, without subsequent purification steps. We now report on new ways for synthesizing poly(anhydrides) using dicarboxylic acid chloride, phosgene, or diphosgene as coupling agents and a removable acid acceptor to effect a one-step polymerization of dicarboxylic acids. These coupling agents are suitable for one-step polymerizations whereby the only byproduct formed is a hydrochloric acid–acid acceptor salt. This acid acceptor is typically an amine base or potassium carbonate. This salt can be removed from the polymerization mixture by either (1) using an insoluble acid acceptor (e.g., cross-linked polyamides, inorganic bases) (eq 1) or (2) using solvents that dissolve exclusively either the poly(anhydride) or the hydrochloric acid–acid acceptor salts (eq 2). In both cases, the byproduct or the precipitating polymer is isolated by simple filtration.

In this study we investigated two approaches for one-step solution polymerization using phosgene, diphosgene, and sebacoyl chloride as coupling agents. In the first approach the effects of various insoluble bases (e.g.,



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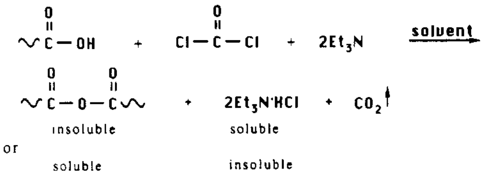

(2)

poly(4-vinylpyridine), K_2CO_3) on the purity and molecular weight of the formed poly(anhydrides) were studied. In the second approach different solvent systems were examined. In these solvents during the polymerization the polymer is separated into one reaction phase (e.g., precipitating solid or soluble) while the formed acid acceptor–hydrochloric acid complex is separated into the other phase.

Experimental Section

Materials. The following compounds were used: phosgene gas (Mathason, MA), diphosgene (Thiokol, MA), cross-linked poly(4-vinylpyridine) (PVP), sebacic acid, sebacoyl chloride, adipic acid, dodecanedioic acid, terephthalic acid, 1,4-phenylenedipropionic acid, triethlamine (TEA), pyridine, tetramethylethylenediamine (TMEDA) (all from Aldrich, Milwaukee, WI). The amine bases were dried over KOH and freshly distilled prior to use. Solvents: dioxane, toluene, *N,N'*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and toluene (gold label, Aldrich, Milwaukee, WI). Chloroform and hexanes (petroleum ether) were dried over activated alumina (ICN Biomedical, Eschwege, West Germany) and distilled before use. All experiments were performed under anhydrous conditions.

1,3-Bis(*p*-carboxyphenoxy)propane was synthesized according to Conix[15] and purified by extraction with acetone followed by extraction with ether prior to use. Phosgene solution was prepared by bubbling phosgene gas into toluene and adjusting the concentration to 1.0 M by dilution. The concentration of this solution was determined by titration with a standard solution of 0.1 N NaOH.

The poly(anhydride) hydrolytic degradation was followed by measuring the UV absorption on a Perkin-Elmer Lambda 1A spectrophotometer (Perkin-Elmer, MA). Circular disk matrices (14 × 1 mm) were prepared by compression molding of the poly(anhydride) (200 mg) in a Carver press at 10 000 psi for 10 min. The devices were placed in a sodium phosphate buffer solution (0.1 M, pH 7.4, 10 mL) at 37 °C, and the degradation rate was followed by measuring the absorbance of the periodically changed solutions at 247 nm.

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 weight of the polymers was estimated on a Perkin-Elmer GPC system (Perkin-Elmer, MA) consisting of the Series 10 pump and the 3600 Data Station with the LKB 214 rapid spectral detector at 254-nm wavelength. Samples were eluted in chloroform (alcohol free) through two PL gel columns (Polymer Laboratories; 100-Å and 1000-Å 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 weight between 500 and 140 000) by using CHROM 2 and GPC 4 computer programs (Perkin-Elmer, MA). Elemental analysis were performed by Galbraith Laboratories (Knoxville, TN). ^{1}H NMR spectra were obtained on a varian 250-MHz spectrophotometer using chloroform-d_1 as a solvent and tetramethylsilane (TMS) as an internal reference.

Solution Polymerization. To a stirred solution of diacid (1 equiv) and base (2.5–3 equiv) in an organic solvent was added the coupling agent (1 equiv) (e.g., sebacoyl chloride, phosgene, or diphosgene) dropwise. The reaction was stirred for 3 h at 25 °C. When either PVP or K_2CO_3 were used as an acid acceptor, the insoluble solids (e.g., PVP·HCl, KCl) were removed by filtration. The filtrate was added dropwise to excess petroleum ether causing the polymer to precipitate. The precipitated polymer was isolated by filtration and dried in a vacuum oven for 24 h at 40 °C. When either triethylamine (TEA) or pyridine was used, the polymerization reaction was quenched in petroleum ether and the poly(anhydride) precipitated from solution. The precipitated polymer was redissolved in chloroform and washed rapidly with a cold acetic acid (pH 6). The chloroform solution was dried over $MgSO_4$, and the polymer was precipitated by adding its solution dropwise to petroleum ether. When toluene, DMF, DMSO, and dioxane were used with TEA as a base, the precipitating solids were removed by filtration and analyzed (Table I). The filtrate was evaporated to dryness in vacuo at 25 °C. The resulting solid was purified by precipitation in petroleum ether from chloroform. The precipitated polymer was isolated by filtration and washed with diethyl ether to remove traces of diphosgene. The reactions between sebacic acid (1 equiv) and sebacoyl chloride (1 equiv) were performed in chloroform and toluene in the presence of either PVP or TEA. The reaction was analyzed as described above (Table II). In a typical polymerization, diphosgene (0.5 g, 0.5 equiv) was added dropwise into a stirred mixture of sebacic acid (2.02 g, 1.0 equiv) and poly(4-vinylpyridine) (3 g, 2.5 equiv) in 20 mL of chloroform. After 3 h at 25 °C, the insoluble PVP·HCl was removed by filtration. The filtrate was quenched in petroleum ether (100 mL). The precipitated polymer was isolated by filtration, washed with anhydrous diethyl ether, and dried for 24 h at 40 °C in a vacuum oven.

Insoluble poly(anhydrides) [poly(1,3-bis(*p*-carboxyphenoxy)-propane) or poly(terephthalic anhydride)] were polymerized as above, but only soluble amines (TEA or pyridine) were used. The polymers precipitated during the reaction and were isolated by filtration (Table III).

The starting material, *N*-carbobenzoxy-L-phenylalanyl-L-glutamic acid, for the synthesis of poly(*N*-carbobenzoxy-DL-phenylalanine glutamic anhydride) was synthesized according to Bodansky.[16] This monomer (1.0 g, 2.5 mmol) was dissolved in a solution of TEA (0.51 g, 5 mmol) in chloroform (10 mL) followed by a slow addition of diphosgene (1.25 mmol) over 15 min. The resulting poly(anhydride) was isolated and purified as above (Table III).

Results and Discussion

Poly(anhydrides) were synthesized by using any of the following coupling agents: (1) dicarboxylic acid chloride (e.g., sebacoyl chloride), (2) phosgene, either as a gas or in solution, or (3) diphosgene. On the basis of the mechanism proposed for the reactions of phosgene[18] and diphosgene,[11] the suggested polymerization mechanism is described in eq 3.

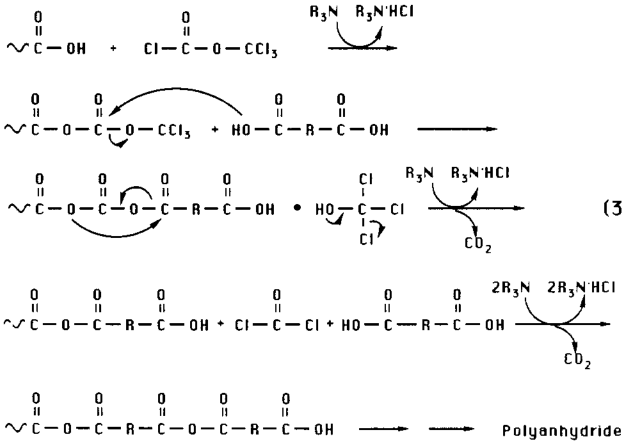

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Table I
Polymerization of Sebacic Acid in Various Solvents

monomer	solvent	anal. of soln[a]	anal. of solid[b]	yield[c] (%)	mp[g] (°C)
SA	chloroform[e]	PSA/TEA·HCl		*d*	78–185[h]
	toluene[e]	PSA	PSA + TEA·HCl	20	78–79
	N,*N*′-dimethylformamide	PSA	TEA·HCl	97	80–81
	dimethyl sulfoxide				
	pyridine	PSA/TEA·HCl		*d*	74–180[h]
	dioxane	PSA/TEA·HCl	TEA·HCl	*d*	
CPP	chloroform	TEA·HCl	PCPP	100	265
TPA	chloroform	TEA·HCl	PTPA	100	>300

[a] The solvent was evaporated and the residue was analyzed. [b] Analysis of the precipitating solid. [c] Pure polymer. [d] Yield cannot be determined due to the presence of TEA·HCl. [e] Polymerized by either diphosgene or sebacoyl chloride as coupling agents. [f] Abbreviations: CPP, 1,3-bis(*p*-carboxyphenoxy)propane; TPA, terephthalic acid. [g] Melting point of the isolated solid from the solution. [h] Melting point of TEA·HCl is 261 °C.

Table II
Presence of Amine–Hydrochloride in the Polymerization Product of the of SA Prepared by Various Methods

polymerization method[a]	yield (%)[e]	IR[b]	TEA:PSA ^{1}H NMR[c]/Elemental	GPC[d]	mp (°C)	elemental anal. (%N, % Cl)
A	f	+	4.3:1/3.5:1	+	70–185[g]	7.21, 19.63
B	62	–		–	81–82	0.18, <0.10
C	f	+	1.9:1/2.4:1	+	68–185[g]	5.26, 3.14
D	65	–		–	81–83	0.11, 0.027
E	60	–		–	81–83	0.11, 0.015

[a] Abbreviations: A, TEA/diphosgene; B, PVP/diphosgene; C, TEA/sebacoyl chloride; D, PVP/sebacoyl chloride; E, regenerated PVP/diphosgene. [b] Typical absorbance of $Et_3N\cdot HCl$ follows (film cast): 2740 (w), 2600 (s, br), 2530 (w, sh), 2500 (s, sh) cm^{-1}.[17] [c] ^{1}H NMR of $Et_3N\cdot HCl$ follows ($CDCl_3$): δ 3.11 (q, 2, $J = 7.3$ Hz), 1.42 (t, 3, $J = 7.3$ Hz). ^{1}H NMR of PSA follows ($CDCl_3$): δ 2.45 (t, 4, $J = 7.3$ Hz), 1.66 (br t, 4, $J = 7.3$ Hz), 1.33 (br s, 8). [d] Sharp peak at retention time = 12.3 min. [e] Pure poly(sebacic acid). [f] Yield cannot be determined due to the presence of TEA·HCl. [g] Melting point of TEA·HCl is 261 °C.

Table III
Poly(anhydride) Synthesis Using Phosgene and Diphosgene as Coupling Agents[a]

acid	coupling agent	acid acceptor	mol wt $\bar{M}_w$	mol wt $\bar{M}_n$	IR (cm^{-1})	mp (°C)
adipic acid	P	TEA	7600	3350	1820, 1735	70–73
adipic acid	P	PVP	8300	3600	1810, 1740	70–74
adipic acid	D	TEA	6900	3200	1820, 1740	69–73
dodecanoic acid	P	TEA	14100	6500	1810, 1740	92–95
dodecanoic acid	P	PVP	12600	5900	1810, 1740	90–95
dodecanoic acid	D	PVP	13750	4800	1805, 1740	92–94
terephthalic acid[b]	P	TEA			1780, 1735	>300
terephthalic acid	P	pyridine			1780, 1735	>300
terephthalic acid[b]	D	TEA			1780, 1730	>300
PDP	P	TEA	8400	3650	1800, 1735	98–101
PDP	P	PVP	7950	2100	1805, 1740	100–102
PDP	D	TEA	9200	2350	1805, 1735	98–102
CPP[b]	P	TEA			1780, 1730	262–265
CPP[b]	P	TEA			1780, 1735	265–266
CPP[b]	D	TEA			1780, 1735	264–266
PHE–GLU	D	TEA	7500	2800	1800, 1740	
PHE–GLU	D	PVP	4680	2400	1800, 1740	

[a] See Table IV. [b] Polymers are insoluble. [c] Abbreviations: P, phosgene solution; D, diphosgene; PDP, phenylenedipropionic acid; CPP, 1,3-bis(*p*-carboxyphenoxy)propane; GLU–PHE, N-carbobenzoxy-L-phenylalanyl-L-glutamic acid.

The results of the polymerization of sebacic acid, as a model, using either phosgene or diphosgene as coupling agents with various acid acceptors are presented in Table IV. Poly(sebacic anhydride) (poly(SA)) with a weight average molecular weight up to 16,300 was obtained. The results are similar for the polymerization of sebacic acid with either coupling agent, phosgene or diphosgene. All the poly(SA) formed had the same melting point and the same IR absorbance characteristics of anhydride bonds. Insoluble amine, PVP, as well as soluble amines (e.g., TEA, pyridine, TMEDA) was used. The formed polymers have similar molecular weights, which indicates a similar activity of the different amine bases as acid acceptors. PVP, as a heterogeneous acid acceptor, did not affect the polymerization (Table IV, runs 4, 6, and 9). However, the nonamine heterogeneous base K_2CO_3 gave a lower molecular weight polymer. This may be explained by the observation that pyridine forms a 1:1 complex with acid chlorides prior to their reaction with hydroxyl-bearing molecules.[8] In the same way, the amines formed a soluble intermediate complex of acid–amine[17] which improved the interaction with the coupling agent under homogeneous conditions. Although the PVP is insoluble in the reaction medium, it swells and forms a similar acid–PVP complex. K_2CO_3, however, forms a heterogeneous mixture with the acid and thus presumably reacts slower with the coupling agents to form the polymer.

A comparative study of the purity of poly(SA) synthesized using soluble and insoluble amines (TEA and PVP, respectively) with diphosgene or sebacoyl chloride

Table IV
Polymerization of Sebacic Acid Using Phosgene and Diphosgene as Coupling Agents[a]

coupling agent	acid acceptor	mol wt		IR (cm^{-1})	mp (°C)
		$\bar{M}_w$	$\bar{M}_n$		
phosgene soln	TEA[b]	14800	6250	1800, 1740	75–77
phosgene soln	pyridine[b]	13700	5950	1800, 1735	76–78
phosgene soln	TMEDA[b]	16300	6600	1805, 1735	76–78
phosgene soln	PVP	13950	5350	1805, 1735	80–81
phosgene gas	pyridine[b]	14100	6820	1805, 1735	75–77
phosgene gas	PVP	13200	6150	1800, 1735	79–80
diphosgene	TEA[b]	12250	5780	1805, 1735	76–78
diphosgene	pyridine[b]	14300	6100	1805, 1740	75–78
diphosgene	PVP	10900	5300	1800, 1735	79–80
phosgene soln	K_2CO_3	6200	2700	1800, 1740	76–78
diphosgene	K_2CO_3	6900	3500	1800, 1740	77–78

[a] Polymerization in chloroform, at 25 °C, for 3 h. [b] Molecular weight and IR spectra were taken of the crude polymer. The IR spectra contained amine·HCl absorbance peaks at 2900–2600 cm^{-1}. GPC output contained an isolated peak atributed to the amine·HCl salt (Figure 1). MW was determined for the polymer peak only. The melting point was determined for the pure polymer.

as coupling agents is presented in Table II. The purity of the polymerization product was determined by spectroscopy (IR, ^{1}H NMR), GPC, melting point determination, and elemental analysis. When soluble base (e.g., TEA) was used as an acid acceptor, the polymer contained a significant amount of TEA·HCl salt (Table II, runs 1 and 3). The relative amount of this salt to the polymer was 4:1 and 2:1 for the coupling agents diphosgene and sebacoyl chloride, respectively. When PVP was used as an acid acceptor for both coupling agents (e.g., diphosgene and sebacoyl chloride), a pure (>99.7%) poly(SA) was obtained. A further advantage for the use of PVP is the ability to regenerate it by neutralization with a sodium bicarbonate solution. The recycled PVP showed similar activity as an acid acceptor (Table II, run 5) and formed a poly(anhydride) identical with the poly(anhydride) synthesized by the initial PVP (Table II, run 2). Poly(SA) prepared with PVP showed a sharp melting point (Table II, runs 2, 4, and 5, mp 81–82 °C (lit.[5] mp 81 °C)). On the other hand, polymers prepared with TEA had a broad melting point due to the presence of TEA·HCl (mp 261 °C). Attempted purification of polymers synthesized with TEA as an acid acceptor (Table II, runs 1 and 3) by rapid water extraction resulted in a decrease in molecular weight and hydrolysis as evidenced by GPC and IR spectra. The IR spectra of the polymer before and after purification revealed the disappearance of the amine salt (2740–2500 cm^{-1}) and appearance of the acid (1680 cm^{-1}). The IR spectra of poly(anhydrides) prepared with PVP as an acid acceptor revealed pure unhydrolyzed polymer.

A second approach to one-step synthesis of pure poly(anhydrides) was the development of a solvent system where the polymer is in one reaction phase (e.g., precipitating solid or solution) and the amine–hydrochloride acid complex is separated into the other phase. Table I describes polymerization of SA in several solvents with TEA as an acid acceptor. Good yields of poly(anhydrides) were obtained in toluene and in DMF. The use of TEA in toluene or DMF is complimentary to the use of PVP in chloroform. In both approaches the poly(SA) is soluble in the reaction media. The insoluble hydrochloric acid–acid acceptor complex, whether an insoluble amine (e.g., PVP·HCl) or TEA·HCl salt, was removed by a filtration, leaving a pure (>99.7%) polymer.

Although in both approaches pure poly(anhydrides) have been obtained with similar molecular weights, the isolation of the polymer by the first approach is preferred.

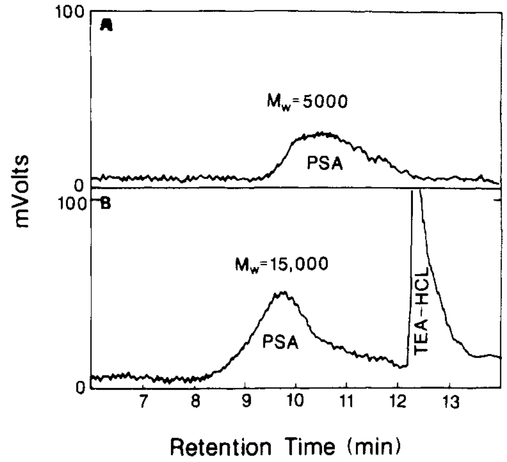

Figure 1. Poly(sebacic anhydride) polymerized in toluene: A, polymer isolated from solution; B, precipitated fraction.

In the second approach high boiling point solvents (DMF or toluene) had to be removed at ambient temperature in order to avoid decomposition of the formed poly(anhydride). An elemental analysis of the poly(SA) formed in DMF (Table I, run 3) revealed trace amounts of amine salt. (Anal. Calcd. for TEA·HCl: N, 2.18; Cl, 5.5). Found: N, 2.18; Cl, 6.01. Yet, the recovered yield was high. The low yield of the isolated poly(SA) in toluene was attributed to the poor solubility of the high molecular weight fractions of the polymer in toluene; this fraction was found in the precipitating salts as demonstrated by GPC (Figure 1). The precipitating polymers had a weight average molecular weight ($\bar{M}_w$) of 15000 but contained TEA·HCl while the soluble polymer had a $\bar{M}_w$ of 5000. When invert partitioning was applied, the polymers were precipitated from the solution while the amine salts remained in solution (Table I, runs 7 and 8). 1,3-Bis(*p*-carboxyphenoxy)propane (CPP) and terephthalic acid (TPA) were polymerized in chloroform by using a soluble acid acceptor (e.g., Et_3N). The formed poly(anhydrides) were insoluble in chloroform and precipitated, while the byproduct ($Et_3N·HCl$) was soluble. After filtration 100% of highly pure polymers (>99.7%) with 100% yield were obtained.

The results in Table IV indicated that either soluble amine base or PVP could be used successfully as hydrochloride acid acceptors to yield polymers with MW up to 16300. On the basis of these results, we synthesized a variety of poly(anhydrides) by using either phosgene or diphosgene (Table III). The aliphatic and the aromatic polymers exhibited a typical anhydride absorbance in the IR spectral at ca. 1800 and 1735 cm^{-1} and at 1780 and 1735 cm^{-1}, respectively.[1] The molecular weights obtained in this study were higher than molecular weights previously reported for solution polymerization.[6-9] However, relatively low molecular weights were obtained for poly(adipic anhydride) and poly(1,4-phenylenedipropionic anhydride). GPC analysis of both polymers revealed the existence of low molecular weight fractions. These unique sharp peaks for both poly(adipic anhydride) (peak at $\bar{M}_n$ of 150) and poly(1,4-phenylenedipropionic anhydride) (peak at $\bar{M}_n$ of 400) affect the polymer molecular weight. These peaks may be the cyclic anhydride dimer form of 1,4-phenylenedipropionic acid (fw = 222) and cyclic anhydride monomer of adipic acid (fw = 150). Similar results were reported in the melt polymerization.[5,19] The utility of this solution polymerization for heat-sensitive diacids was demonstrated in the synthesis of a polyanhydride from *N*-carbobenzoxy-L-phenylalanyl-L-glutamic acid (Table III, runs 16, and 17). A pure polymer with a characteristic anhydride IR absorbance was obtained. Attempted polymerization of this dipeptide by the melt condensation yielded a tar.

Since these polymers are considered as biodegradable materials, we have studied their degradation characteristics under physiological conditions (sodium phosphate buffer 0.1 M, pH 7.4, 37 °C). Thick films (1 mm) of aliphatic poly(anhydrides) of adipic acid, sebacic acid, and dodecanedioic acid were completely degraded after 5, 12, and 18 days, respectively. Thick films (1 mm) of aromatic polymers of terephthalic acid and CPP showed a weight loss of 33% and 24%, respectively after 3 months.

A comparative stability study of storage under anhydrous conditions was performed. Poly(SA) prepared by the new method, using PVP, was stable under storage. On the other hand, poly(SA) prepared with TEA followed by water extraction of the TEA·HCl salt was hydrolyzed under storage to an insoluble solid within 1 week. This instability was attributed to the polymer hydrolysis by water molecules entrapped in the polymer bulk during purification.

This study presents one-step polymerization of poly(anhydrides) by solution polymerization at ambient temperature. Either phosgene or diphosgene proved convenient to synthesize pure poly(anhydrides); however, diphosgene is the preferred coupling reagent. In contrast with the traditional use of dehydration agents, the use of insoluble acid acceptors (PVP or inorganic bases) yielded highly pure polymers. The use of various solvent systems is complimentary to the use of the insoluble bases in chloroform. The choice of the right solvent system can be used for precipitating exclusively either the polymer or the amine–acid salt; thus, filtration leads to pure polymers. These methods are advantageous for the polymerization of heat-sensitive dicarboxylic acids such as therapeutically active diacids and poly(anhydrides) of dipeptides.

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Registry No. Phosgene, 75-44-5; diphosgene, 503-38-8; sebacoyl chloride, 111-19-3.

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New Polymer Syntheses. 24. Liquid Crystal Poly(ester imides) Derived from Benzophenonetetracarboxylic Dianhydride and ω-Amino Acids

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ABSTRACT: Six dicarboxylic acids were prepared from benzophenone-3,3′,4,4′-tetracarboxylic dianhydride (BTA) and 4-aminobutyric acid, 5-aminovaleric acid, 6-aminocaproic acid, 7-aminoheptanoic acid lactam, 11-aminoundecanoic acid, and 12-aminododecanoic acid. These diacids were condensed with the diacetates of hydroquinone, 2,6-dihydroxynaphthalene or 4,4′-dihydroxybiphenyl. The resulting poly(ester imides) were characterized by inherent viscosity elemental analyses, differential scanning calorimetry (DSC), observation under polarized light, and WAXS measurements. Formation of a smectic melt was found for almost all polymers containing 4.4′-dihydroxybiphenyl. These thermotropic poly(ester imides) were also characterized by thermomechanical and thermogravimetric analyses, and an odd–even effect was found for the heat-distortion temperatures. Only one poly(ester imide) of hydroquinone formed a mesophase. Because in this case no component of the polymer chain is a mesogen, the formation of a mesophase indicates a special cooperative effect, presumably a charge-transfer interaction, between the aromatic monomer units.

Introduction

In a previous part of this series[1] poly(ester imides) derived from pyromellitic anhydride (PMA), ω-amino acids, and various bisphenols, in particular hydroquinone (**1a–d**) or 4,4′-dihdyroxybiphenyl (**2a–d**) were described. These poly(ester imides) were investigated with regard to the formation of mesophases and with regard to their thermomechanical properties. Two interesting results were obtained. First, the polymers **2a–d** did not form a well-defined mesophase, although the 4,4′-dihydroxybiphenyl unit is well-known as a mesogenic group.[2,3] Surprisingly, poly(ester imides) containing hydroquinone (e.g., **1c**) or