Synthesis and Characterization of Fumarate-Based Polyesters for Use in Bioresorbable Bone Cement Composites

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Received 5 March 1997; accepted 3 May 1997

ABSTRACT: Fumarate-based polyesters were prepared by the transesterification polycondensation of diethyl fumarate and diols: (±)-1,2-propanediol, (S)-(+)-1,2-propanediol, 2-methyl-1,3-propanediol, and 2,2-dimethyl-1,3-propanediol. Different polyester microstructures were observed by ^{1}H-NMR and ^{13}C-NMR spectroscopy when the reaction was conducted in the presence of *p*-toluenesulfonic acid monohydrate or metal containing catalysts—aluminum trichloride, titanium tetrachloride, titanium tetrabutoxide, and zinc chloride. The extent of formation of branched structures associated with hydroxyl end groups' addition to the unsaturated polyester double bonds depends on the acidity of the catalyst. The bone cement composites were prepared by mixing the fumarate polyesters with an inorganic filler, $CaSO_4 \cdot 2H_2O$, and *N*-vinyl pyrrolidone, which crosslinks on the addition of a radical initiator, benzoyl peroxide, at ambient temperatures. The compressive strength and hydrolytic stability of the cement compositions was correlated with structure of the polyesters. © 1997 John Wiley & Sons, Inc. J Appl Polym Sci **66:** 1123–1137, 1997

Key words: fumarate polyesters; bioresorbable bone cement composites

INTRODUCTION

The field of biodegradable polymers is a fast growing area of polymer science because of the interest of such compounds for temporary surgical and pharmacological applications. Recent reviews identify the family of aliphatic polyesters as the most attractive and promising among polymers degradable in model aqueous media or in animal bodies.[1,2] Of particular interest are bioresorbable polyesters which can degrade and further resorb *in vivo,* i.e., which are eliminated through natural pathways either because of simple filtration of degradation by-products or after their metabolism with no residual side effects.[1] Linear aliphatic polyesters, especially poly(glycolide), poly(lactide), and poly(ϵ-caprolactone), have proven to be effective polymers in several surgical applications, including sutures, bone plate, and controlled drug delivery systems.[3–5] These polymers are biodegradable, and they produce by-products that are completely biocompatible.

Crosslinkable polyesters having various functional groups have been investigated as part of

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Journal of Applied Polymer Science, Vol. 66, 1123–1137 (1997)
 CCC 0021-8995/97/061123-15

biodegradable composite materials for custom-formable fixation devices.[6,7] Unsaturated polyesters have been considered as potential matrices in bioresorbable composites and bone cement.[8,9] Poly(methyl methacrylate) (PMMA), the current standard for bone cement, provides immediate structural support, but being biologically inert, acts as a barrier to new bone ingrowth.[10,11] Furthermore, an appropriately immobilized fracture should heal within several months, after which the PMMA-based device becomes unnecessary and would require a second surgical procedure for removal. A biodegradable cement would have the same advantages as PMMA during the initial postoperative period. However, with the progression of healing, the biodegradable cement could slowly degrade and thereby avoid interference with progressive bone regrowth. Thus, with time, the increasing rigidity of the healing bone would take over the function of the resorbed cement.

One particularly promising polymer for this application is an unsaturated polyester, poly(propylene fumarate) (PPF), as follows:

$$-(-CH_2-CH(CH_3)-OOC-CH=CH-COO)_n-$$

Fumaric acid (HOOC—CH=CH—COOH), a naturally occurring substance, is found in the tricarboxylic acid cycle (Krebs cycle); whereas propylene glycol (1,2-propanediol) is a commonly used diluent in drug formulations. The use of fumaric derivatives in the polyester synthesis allows introduction of an unsaturated site into the polymer; here, there is the additional feature of chemical activation of the double bond by the adjacent carbonyl group, which permits ready crosslinking. Gerhard et al. formulated a biodegradable cement using MMA to crosslink PPF and incorporated antibiotics into the cement before cure.[12] The development of a biodegradable cement was carried further by Wise et al.,[13] who utilized the polyesters prepared by bulk and suspension polymerization of diethyl fumarate and propylene glycol. Sanderson[14] reported use of a PPF crosslinked by vinyl pyrrolidone as cement for controlled drug release. PPF polyesters can be prepared by reacting propylene glycol with fumaric acid, fumaryl chloride, and dicarbodiimide fumarate.[12–16] Oligomers of controlled molecular weight, polydispersity, and polymer end groups were prepared by step polymerization using bis(2-hydroxypropyl fumarate) or propylene bis(hydrogen maleate) as starting materials.[16] The use of higher molecular weight PPF ($>10^4$ g/mol) is considered as important because better mechanical properties can be realized.[17]

The macromolecular design of an improved polymeric material requires a control over the polymer synthesis and an understanding of the effects of polymer structure on its physical properties and degradation. An aspect of these fumarate-based bioresorbable composites that has not been probed is the polyester microstructure and its relation to physical properties and hydrolysis of the cements. In this article, we present results of microstructure analysis of PPF and some fumarate-based polyesters prepared with different catalysts, as well as the impact of the microstructure on their compression strength and hydrolysis of the composites.

EXPERIMENTAL

Polymer Synthesis

Fumarate-based polyesters were synthesized by the transesterification polycondensation of diethyl fumarate (DEF) (Janssen Chimica, New Brunswick, NJ) and a diol, (±)-1,2-propanediol (PD) (Aldrich, Milwaukee, WI); (S)-(+)-1,2-propanediol (SPD) (Aldrich); 2-methyl-1,3-propanediol (MPD) (Aldrich); and 2,2-dimethyl-1,3-propanediol (DMD) (Aldrich) by an adaptation of the procedure described by Sanderson.[14] DEF and the diols were used as received. The diol was used in 10 mol % excess over DEF. The reaction was catalyzed with *p*-toluenesulfonic acid monohydrate (PTSA), $AlCl_3$, $TiCl_4$, $Ti(OC_4H_9)_4$, and $ZnCl_2$ (all supplied by Aldrich). A typical two-stage polymerization involved heating the reagents under a nitrogen sweep to 230–240°C for 6–8 h, during which about 75% of the expected ethanol was collected. A vacuum (1 torr) was then applied at 210°C for 6–8 h to remove any remaining by-products. Precipitation from methylene chloride solution into diethyl ether resulted in a suspension of a polyester that was filtered, washed with fresh diethyl ether, and dried under vacuum at room temperature.

Composite Preparation

A moldable, curable composition was prepared by mixing of 22.7 wt % polyester, 8.5 wt % *N*-vinyl

pyrrolidone (freshly distilled, Aldrich), 0.7 wt % benzoyl peroxide (Aldrich), and 68.1 wt % calcium sulfate dihydrate (Aldrich). When mixed together, the composition becomes a puttylike mixture, which remains moldable for 15–30 min and then cures to a rigid state.

Characterization

The molecular weight of polymers was determined relative to polystyrene standards in chloroform solutions with sample concentrations 0.3% (wt/vol) by gel permeation chromatography (GPC) using a Waters Model 510 pump at an elution rate of 1.0 mL min, and Waters Model 410 refractive index detector with 10^3 through 10^6 Å ultrastyragel columns in series. Injection volumes of 125 mL were used. Polystyrene standards of a low dispersity (Polysciences) were used to generate a calibration curve.

NMR spectra of 4–10% polymer solutions in $CDCl_3$ were recorded at ambient temperature on a Bruker AC-200 spectrometer operating at 200.13 MHz for ^1H and 50.33 MHz for ^{13}C. Chemical shifts are reported referenced to $CDCl_3$. Proton spectra utilized 16 K data points with a sweep width of 3600 Hz adjusted so that no quaditive images affected the spectra. A sweep width of 13.5 kHz and 32 data points were used for the ^{13}C-NMR spectra. The distortionless enhancement by polarization transfer (DEPT) NMR spectra were obtained with evolution delay of 3.704 ms to produce negative methylene and positive methine and methyl ^{13}C resonance signals. $^1H-^{13}C$ correlation spectra were run using the standard XHCOR Bruker program.

Compressive testing for strength and modulus was conducted according to ASTM Standard F 451-756 for acrylic bone cement with the MTS (Q-TEST) materials test system interfaced with a 486 laboratory computer. Samples for testing were prepared by placing the curing composition in cylindrical Teflon molds (6 mm in diameter and 12 mm length specimens) and allowed to harden for 48 h at 37°C. Uniaxial compression tests were conducted at a crosshead rate of 20 mm min. Compressive strengths were determined from the maximum loads achieved divided by the original cross-sectional area (ca. 28 mm^2).

Polymers and composites were degraded in phosphate-buffered saline pH 7.4 in an incubator at 37°C. To determine mass loss during degradation, preweighed disks (6 mm in diameter and 3 mm length) were each placed into a tared scintilation vial. Periodically, the samples were removed from the incubator, rinsed with distilled water, and dried *in vacuo* until a constant mass; and the mass loss was recorded as the average of the three individually degraded samples. The percentage mass loss was determined for each sample by comparing the dry weight (m_d) remaining at a specific time with the initial weight (m_o); % mass loss = $(m_o - m_d)/m_o \times 100$.

Glass transition temperatures (T_g) were determined on a TA Instruments model modulated DSC 2920 with a heating rate of 5°C per minute in the −30 to 120°C range. The T_g was taken as a midpoint of a straight line drawn between the inflection of the peak's onset and endpoint.

RESULTS AND DISCUSSION

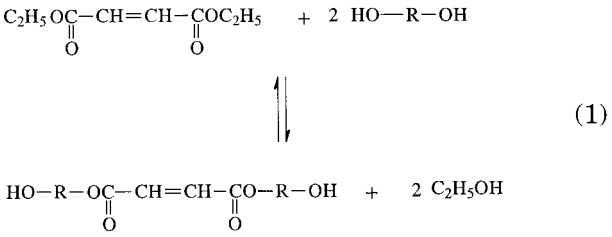
Polymer Synthesis

Fumarate-based polyesters were prepared via an ester exchange reaction with the conditions de-

Table I Polycondensation of DEF and Diols

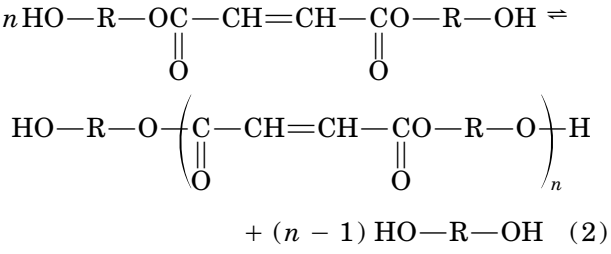
Sample No.	Diol	Catalyst	Time (h)	Maximum Temperature (°C)	Yield (wt %)	$M_w \times 10^{-3}$ (daltons)	MWD	T_g (°C)
1	PD	PTSA	16	240	38	32.6	2.2	23
2	PD	$AlCl_3$	16	230	42	13.7	2.3	14
3	PD	$TiCl_4$	12	200	43	20.9	1.4	14
4	PD	Ti $(OC_4H_9)_3$	12	200	65	15.2	1.4	16
5	PD	$ZnCl_2$	12	200	68	26.6	1.9	16
6	SPD	$ZnCl_2$	12	200	52	67.0	1.3	17
7	MPD	$ZnCl_2$	12	200	77	39.7	1.9	−2
8	DMD	$ZnCl_2$	16	200	66	12.7	1.3	−6

tailed in Table I. DEF first reacts with an excess of diol (R = $CH(CH_3)CH_2$, $CH_2CH(CH_3)CH_2$, $CH_2C(CH_3)_2CH_2$), liberating ethanol and forming a bis(hydroxyalkyl) ester (eq. 1).



(1)

In a second stage, the ester is subjected to polycondensation by alcoholysis,[18] forming the polyester (eq. 2)

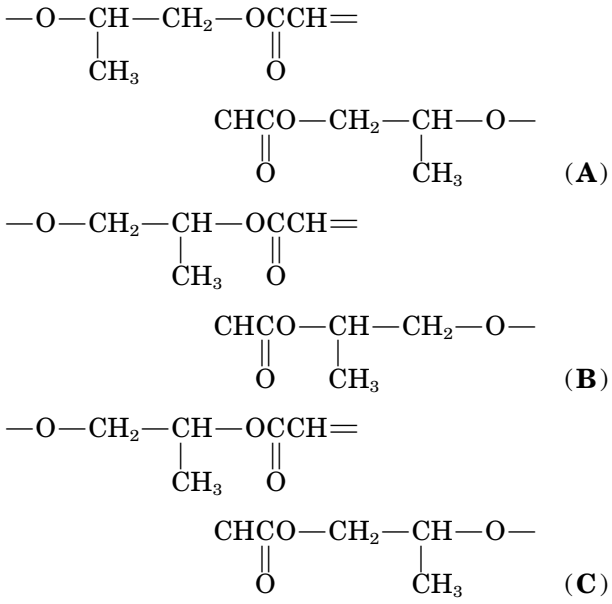


(2)

Both stages are inherently reversible, but the conditions are chosen to drive each reaction in forward direction by removal of the low molecular coproduct as it is formed. A mixture of diethyl fumarate and a diol with a polyesterification catalyst is heated with stirring in an inert atmosphere at 150–200°C until the evolution of ethanol is complete. The process is then continued at higher temperature and under reduced pressure (down to ca. 0.5 mm Hg) to effect polymerization. The diol is used in 10% mol excess over the theoretical requirement of the first step in order to force the ester-exchange reaction toward completion and to compensate for losses of the diol. Losses of glycol with concurrent stoichiometric imbalances are well established in the synthesis and manufacture of propylene glycol-based unsaturated polyesters for molding resins.[19] The losses are typically attributed to the volatility of propylene glycol and its tendency to undergo side reactions such as acid catalyzed dehydration and the formation of cyclic ethers.[20] The choice of final working temperature for the second stage (usually below 210°C) is governed by the need for the product to be kept molten during polymerization.

Catalysts, PTSA,[13,14] as well as Lewis acids like $AlCl_3$, $TiCl_4$, and $ZnCl_2$, accelerate polycondensation of DEF and PD, with least acidic $ZnCl_2$ giving highest yield and molecular weight of the polymer (Table I). Similarly effective is a weak basic catalyst, $Ti(OC_4H_9)_4$.

The studies of the ^1H- and ^{13}C-NMR spectra of the DEF–PD polyesters reveal marked differences in microstructure when PPF is prepared with PTSA or less acidic catalysts, $AlCl_3$, $TiCl_4$, $ZnCl_2$, and $Ti(OC_4H_9)_4$. The ^1H-NMR spectra of the polymers catalyzed with PTSA and $ZnCl_2$ are presented in Figure 1. Spectra of the PPF polyesters prepared with $AlCl_3$, $TiCl_4$, and $Ti(OC_4H_9)_4$ are virtually the same as the one for the polymer prepared with $ZnCl_2$. The peak's assignment of the peaks are based on the 2D $^1H-^{13}C$ and DEPT NMR spectra,[21] as well as spectra of model compounds and literature data.[22–24] The broadening of resonances corresponding to protons of PD units is associated with isomeric PD structures in the polymer. Since the primary and secondary hydroxyl groups of PD react somewhat differently with DEF, the 1,2-propylenedioxy groups derived from them are combined into the polyester chain with random orientations, such that the pendent methyl groups occur at either the head or the tail of successive repeating units, leading to an aperiodic spacing of the methyl groups along the chain (**A, B,** and **C**).



(**A**)

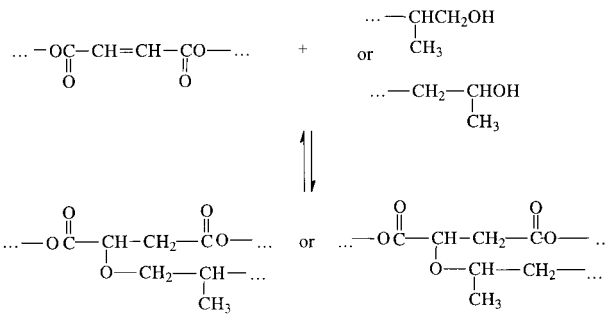
(**B**)

(**C**)

It was suggested that this disturbance of structural regularity is further compounded by the racemic character of commercial 1,2-propanediol,

which leads to a random (atactic) distribution of optical configurations.

The comparison of the two ^{1}H-NMR spectra (Fig. 1) indicates that catalysis with PTSA results in a polyester with more complex NMR spectrum. In addition to absorption peaks assigned to DEF and PD residues in structures **A–C,** peaks in the 2.3–4.9 ppm range reflect structural complexity of the polyesters due to side reactions of the fumarate double bonds. It has been observed[25] that the double bonds disappear in appreciable quantities during synthesis of unsaturated polyesters as the result of the reaction of PD hydroxyl groups or hydroxyl end groups with fumarate double bonds, leading to a variety of branched structures, such as the following:



(D) **(E)**

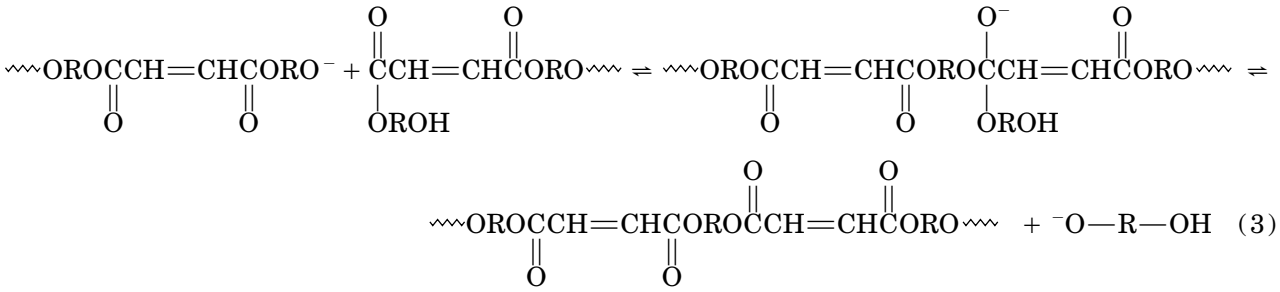
Two-dimensional ^{1}H and ^{13}C-NMR spectra[21] and studies of model compounds[22] have suggested that the lower and higher field bands of the two bands centered at 2.9 ppm can be assigned to main chain succinic methylene protons of the structures **D** and **E,** respectively; whereas resonances at 3.5–3.7 ppm most likely correspond to the CH_2 and CH protons of etherified PD branches, respectively. Broad resonances in the 4.3–5.0 ppm range correspond to succinic methine protons (**D** and **E**). Small absorption at 6.2 ppm corresponds to a small fraction of maleic double bond protons. It is evident that the contribution of the branched structures to the microstructure of PPF obtained with PTSA is much higher than in PPF obtained with $ZnCl_2$ (Fig. 1).

Integration of the proton resonances in the polymer spectra provided a relative estimate of chemical composition as well as the relative extent of the addition side reaction. Thus, hydroxyl end group addition to unsaturated polyester double bonds involved 25–30% of the fumaric ester residue for PTSA catalyzed PPF and about 3–5% of $ZnCl_2$, $TiCl_4$, or $Ti(C_4H_9)_4$ catalyzed PPF.

It was shown that the extent of the double bond saturation increases with reaction temperature, diol concentration, strength, and concentration of the acid catalyst.[25] Studies on a model compound,[24] bis(hydroxypropyl) fumarate indicated that the addition reaction is reversible, favored by high temperatures and catalyzed by strong acids, such as PTSA, via a carbocationic mechanism.[26] The reaction results in the formation of side chains and in a modification of the stoichiometry due to diol consumption.

Different PPF microstructures are even more evident from the analysis of ^{13}C-NMR and DEPT spectra of the polyesters obtained with PTSA and $ZnCl_2$ (Figs. 2 and 3). Particularly sensitive are PD carbon resonances associated with different placement of PD units in the polyesters' main chain, i.e., for structures **A, B,** and **C.** Thus, methyl carbon peaks at 14.2 and 16.0 ppm and methylene carbon peaks at 61.0 and 66.3 ppm correspond to PD resonances in **A** and **B** structures, respectively.[24] Peaks of PD methine carbons at 65.1 and 69.8 ppm of **A** and **B** structures, respectively, which overlap with the methylene resonances in the 65–75 ppm range (Fig. 2), can be observed better in the DEPT spectra (Fig. 3). The spectrum of PPF ($ZnCl_2$) shows almost exclusively **A** structures, whereas the one of PPF (PTSA) indicates that both **A** and **B** structures are present. There are also several peaks of lower intensity in the 65–75 ppm region, which can be assigned to methylene and methine carbons of branched PD units in structures **D** and **E.** Methylene and methine carbons of succinate groups in structures **D** and **E,** which appear due to the reaction of hydroxyl end groups with fumarate double bonds, are observed at 36.8 and 45.4 ppm, respectively. Owing to the presence of the ester groups of primary (50%) and secondary (50%) alcohols, four main peaks of nearly equal intensities are obtained for the unsaturated carbons of the fumaric unit in 132–134 ppm range. Resonances of fumarate carbonyls appear at 163.2–164.5 ppm, whereas a broader lower field peak in the 167–175 ppm range is indicative of succinic carbonyl groups resulting from the saturation reaction. The comparison of ^{1}H- and ^{13}C-NMR data supports the observation that less acidic catalysts like $ZnCl_2$, $TiCl_4$, and weak basic catalyst $Ti(OC_4H_9)_4$ with coordinating metal atoms lead to selective formation of structures **A.** In this case, DEF has a statistical preference to form esters with the primary hydroxyl group on the

PD molecule, producing corresponding PD fumarate esters with a preponderance of terminal secondary hydroxyl groups. Lewis acids, zinc chloride, and titanium tetrachloride form a complex with the hydroxyls through association with an unshared pair of electrons on the oxygen atom and catalyze alcoholysis via acid catalysis. Titanium butoxide converts the reacting hydroxyl group to the corresponding alkoxide, which is the effective intermediate for the reactions involved in the exchange process[27] (eq. 3), as follows:



(3)

The NMR spectra (Figs. 1–3) also indicate that catalysis with $ZnCl_2$, $TiCl_4$, and $Ti(OC_4H_9)_4$ significantly decreases addition of hydroxyl chain ends to the fumaric double bonds.

The NMR spectra of PPF prepared with optically pure (S)-(+)-1,2-propanediol and $ZnCl_2$ as a catalyst were as well resolved as the spectra of the polyester prepared with the racemic PD, thus indicating a similar microstructure.

Commercially available diols, 2-methyl-1,3-propanediol (MPD) and 2,2-dimethyl-1,3-propanediol (DPD), were used for transesterification with DEF (Table I). To minimize the saturation reaction in the case of polymerization of DEF with MPD and DMD diols, $ZnCl_2$ was used as a catalyst. Since these are symmetrical diols with primary hydroxyl groups, mostly regular polyesters were expected. The ^{1}H- and ^{13}C-NMR spectra of the polymers are presented in Figures 4 and 5. The spectra are well resolved and indicate regular structure.

Polymer Properties

The properties of polyesters are determined by the molecular weight; the proportion of carboxylate ester groups in their structure; and the geometry, polarity, and segmental mobility of their repeating units. Weight-average molecular weight (M_w) and the polydispersity (M_w/M_n) are included in Table I. The fumarate-based polyesters formed by transesterification reaction techniques have the weight-average molecular weight ranging between 12×10^3 and 67×10^3 daltons with a molecular weight distribution (MWD) of 1.3–2.3. An increase in the molecular weight of an unsaturated polyester toward 10^4 g/mol improves its hardness, tensile and flexural strength, and its glass transition temperature.[28] Thus, compressive strength of the bone cement composites consisting of the PPF oligomer, tricalcium phosphate, calcium carbonate, and methyl methacrylate increased as the degree of polymerization (DP) increased, showing maximum strength at 7 MPa at DP = 15.[16] The use of higher molecular weight polyesters ($>10^4$ daltons) is viewed as important because of increased entanglement of the polymer chains and reduced chain end free volume leading to a maximum plateau in mechanical properties.[29]

Mechanical properties of polymeric materials are also associated with the nature of their physical state or morphology. Fumarate polyesters prepared from PD, MPD, and DPD diols are amorphous polymers. The loss of crystallinity is associated with increased intermolecular separation of adjacent chain backbones due to methylene groups and substitution of hydrogen atoms by methyl groups. Glass transition temperature of the polyesters was studied by differential scanning calorimetry (DSC). No melting transition was observed for all the polyesters. The T_g for the respective resins are reported in Table I. The highest T_g was observed for the PTSA-catalyzed DEF–PD polyester. Higher T_g of this DEF–PD polymer in comparison with the polyesters obtained in the presence of metal containing catalysts is apparently associated with the bulky branches (structures **D** and **E**) which restrict the

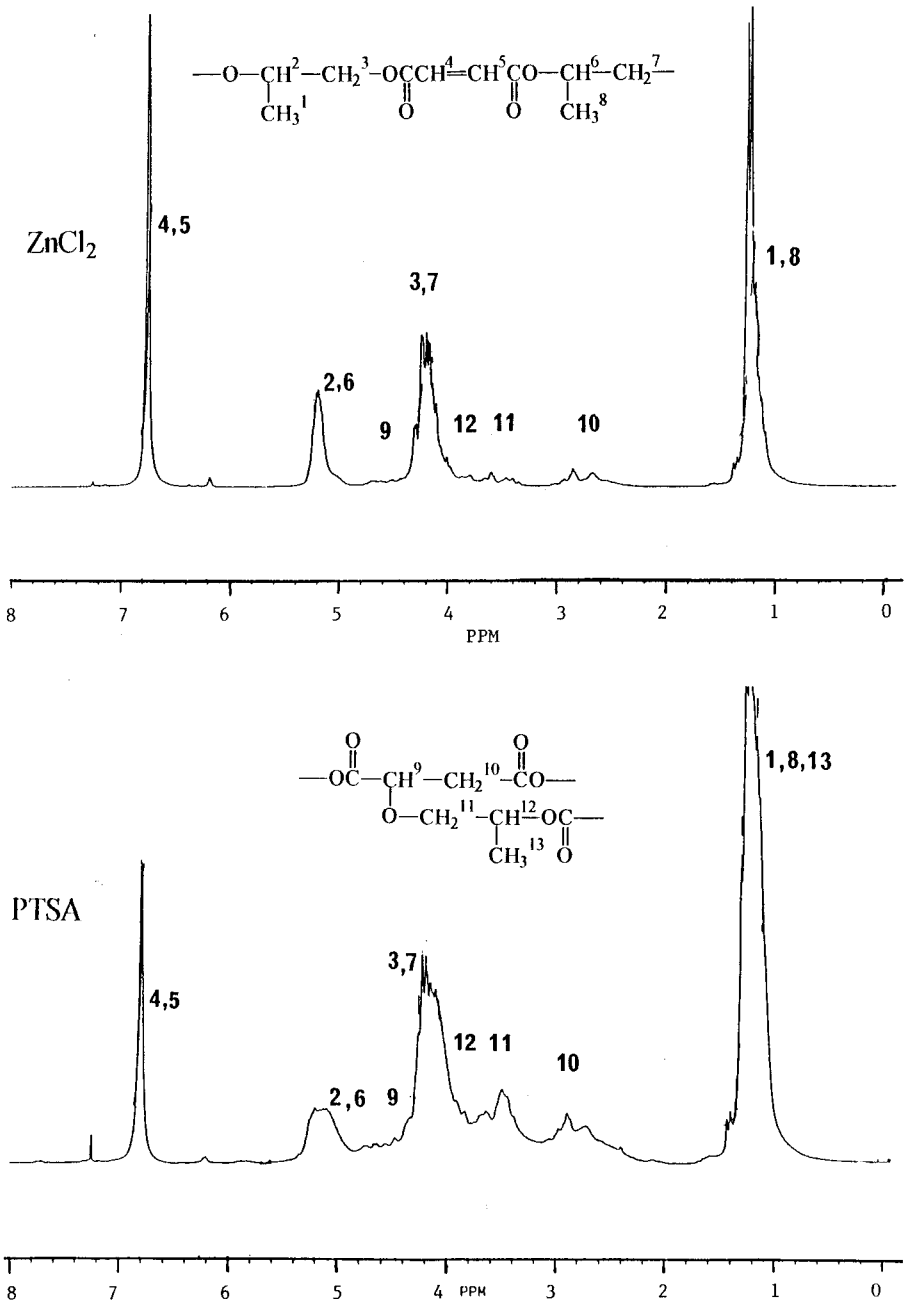


Figure 1 ^{1}H-NMR spectra of PPF polyesters prepared in the presence of $ZnCl_2$ and PTSA.

chain mobility. Addition of a methylene group in the main chain in MPD- and DMD-based polyesters results in lowering the T_g of the polymer.

Bone Cement Composite

Polymer–ceramic composites represent recent advances in resorbable bone cements,[29] which are designed to mimic the viscoelastic properties of bone and improve fracture toughness (i.e., reduce brittleness), resulting in better performance in mixed stress modes and improved initial moldability. In preparing moldable bone replacement material from the fumarate-based unsaturated polyesters, the polymer was mixed with a vinyl monomer, *N*-vinyl pyrrolidone (NVP); a radical

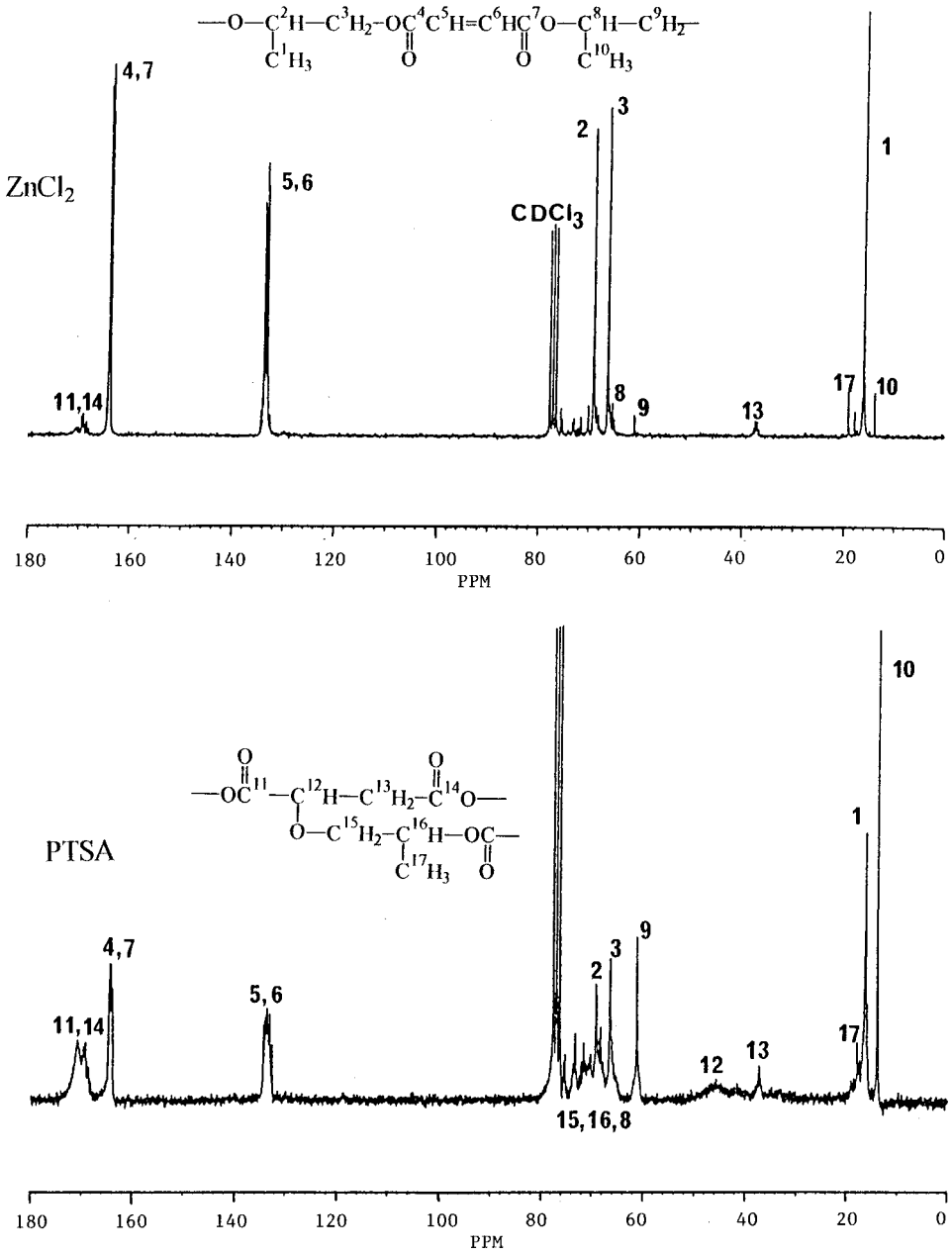


Figure 2 ^{13}C-NMR spectra of PPF polyesters prepared in the presence of $ZnCl_2$ and PTSA.

initiator, benzoyl peroxide; and inorganic filler, $CaSO_4 \cdot 2H_2O$.

The free radicals produced by benzoyl peroxide (2 wt % based on polyester and NVP) initiate crosslinking polymerization involving the fumarate groups in the polyester chains and the unsaturated NVP monomer. As a tertiary amine, NVP, in conjunction with benzoyl peroxide, apparently accelerates free radical formation at ambient temperatures.[19] Crosslinking proceeds rapidly and establishes the structure of the three-dimensional network in which the polyester and NVP are immobilized in an inorganic matrix. The mixture is workable by hand and solidifies in 15–20 min at body temperatures (37°C) to give a cured composite. Unlike the PMMA system,[29] setting is only mildly exothermic, with maximum cure temperatures of 45°C for 20 g material. This is because

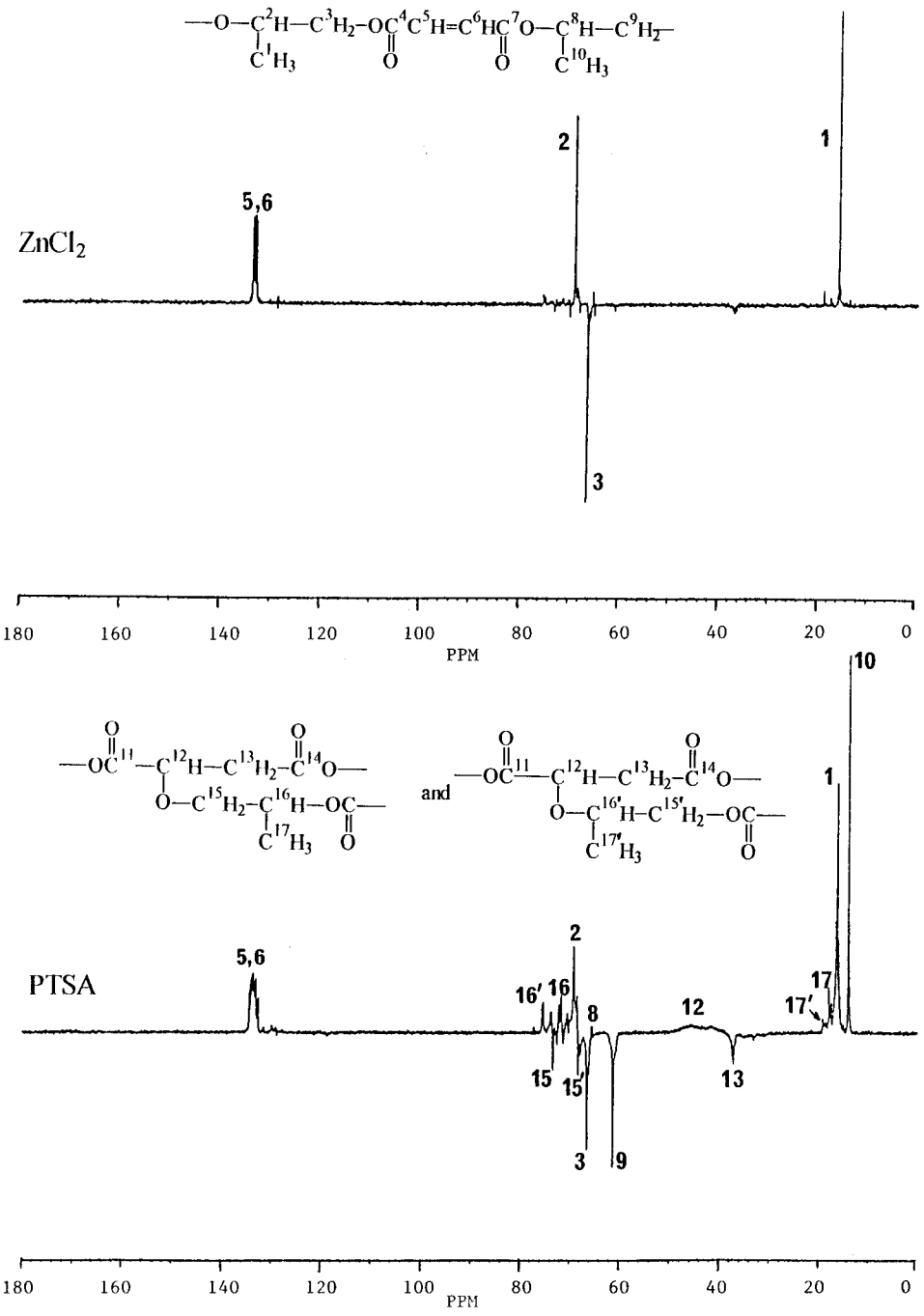


Figure 3 ^{13}C-NMR DEPT spectra of PPF polyesters prepared in the presence of $ZnCl_2$ and PTSA.

a much lower percentage of liquid monomer is undergoing polymerization than in the commercial acrylic systems. The unmodified, cured fumarate-based polyesters are semiflexible material of modest strength and stuffiness. Therefore, in bone cement applications, reinforcing inorganic fillers are required to improve strength and modulus. Additionally, the inorganic filler may act to dissipate some of the polymerization heat and reduce shrinkage of the cement, eliminating internal voids and cracking.[19] Calcium sulfate, both as the hemihydrate and dihydrate, has been used for

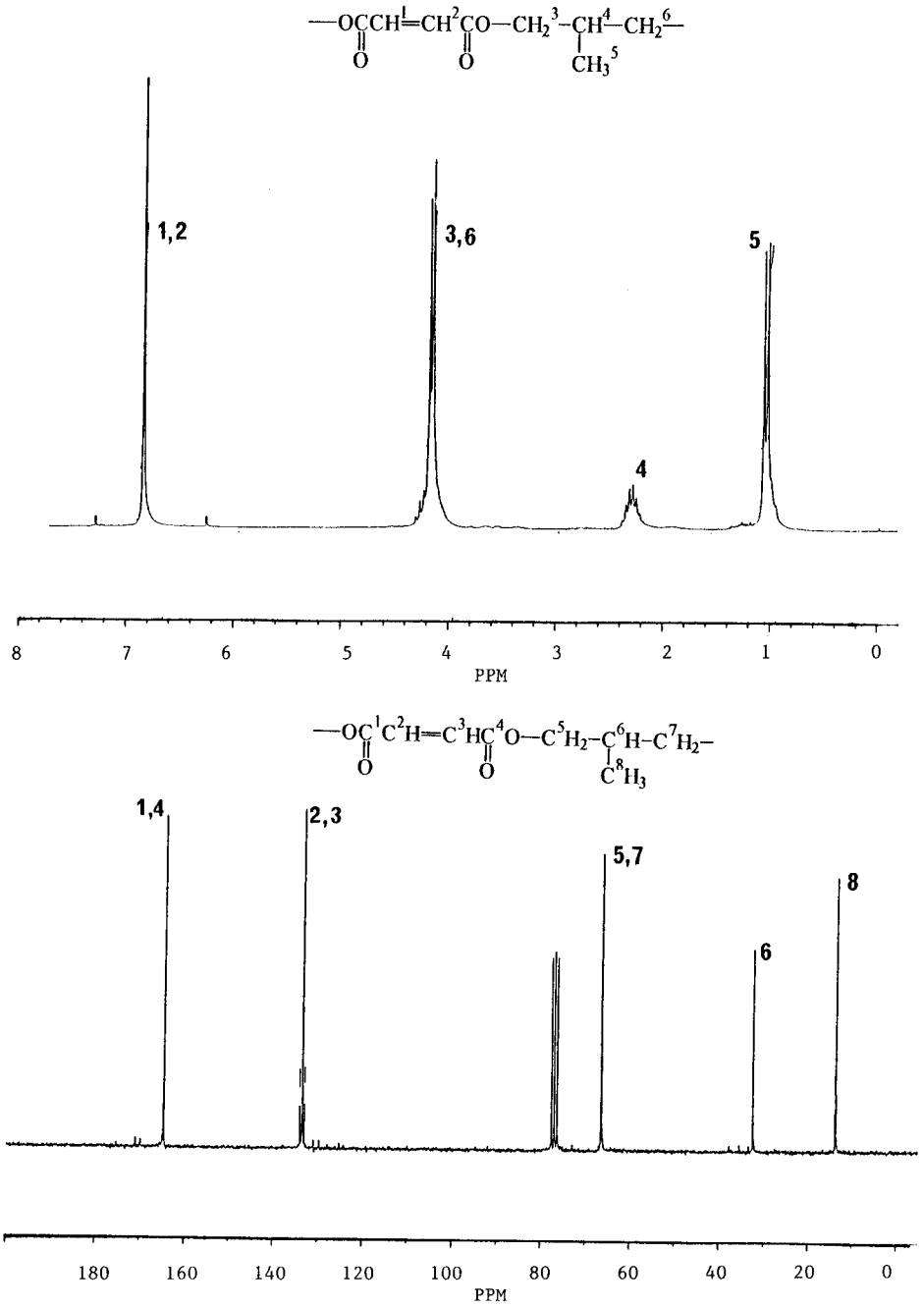


Figure 4 ^{1}H- and ^{13}C-NMR spectra of fumarate polyester prepared with 2-methyl-1,3-propanediol and $ZnCl_2$ as a catalyst.

many years to fill bone defects. Experiments have shown complete resorption in 42–72 days with bone remodeling complete in three months.[30]

To maximize the crosslinking reaction, the weight ratio of PPF to NVP was kept the same for all compositions at 2.64, which corresponds to a stoichiometric relationship of approximately 1.2 NVP units for each fumarate unit. Optimum compression strengths were obtained around this ratio, which is close to the one for commercial fumarate polyester resins usually containing 30–45% styrene.[28] In this case, it was shown that styrene does not enter into homopolymer formation independent of crosslinking. No polystyrene polymers

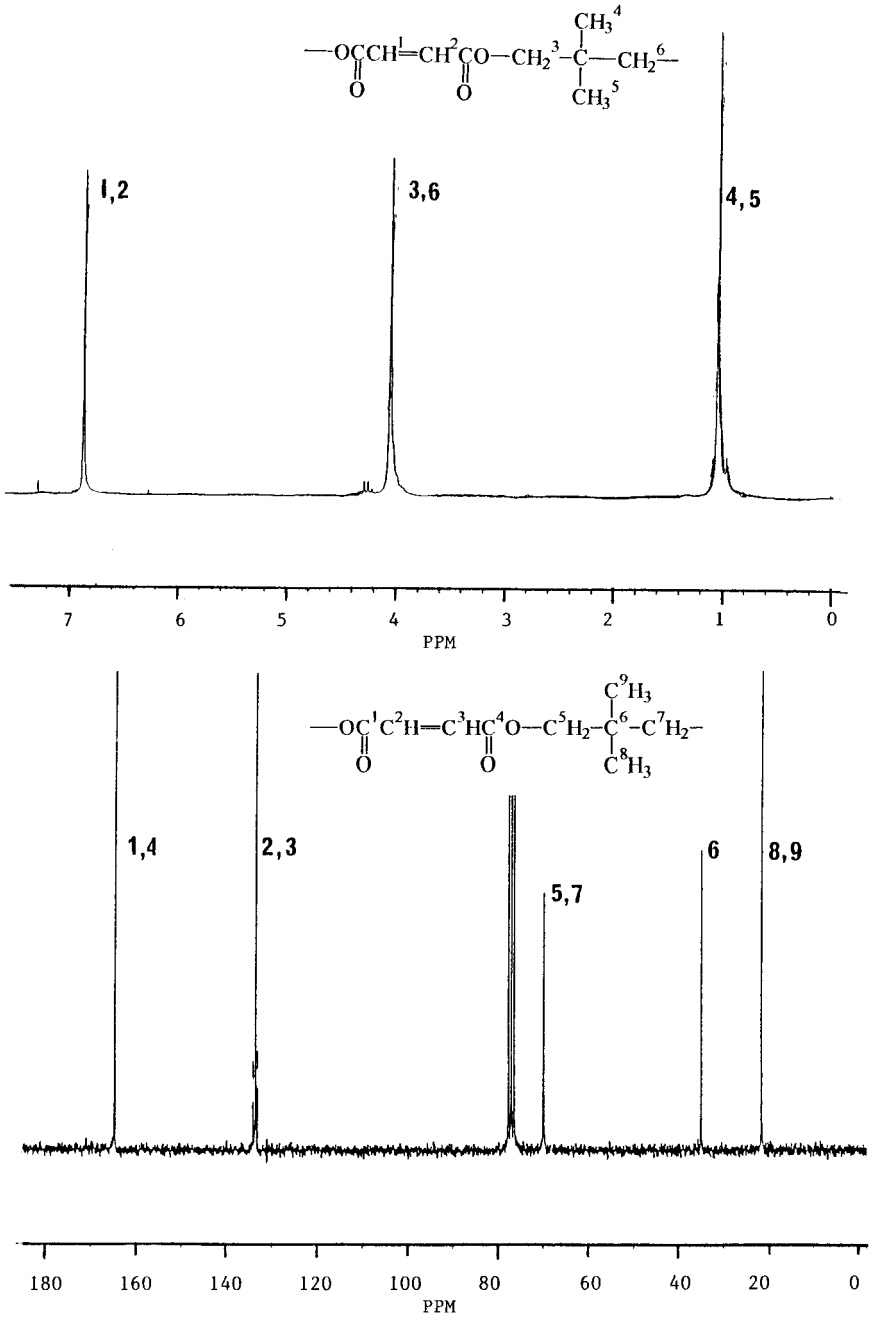


Figure 5 ^{1}H- and ^{13}C-NMR spectra of fumarate polyester prepared with 2,2-dimethyl-1,3-propanediol and $ZnCl_2$ as a catalyst.

have been extracted, even in polyester resins containing 60% styrene monomer. In a recent curing study of PPF (M_w = 6650)–NVP–hydroxyapatite cement, Gresser et al.[31] have found that through a range of PPF/NVP weight ratios from 0.33 to 2.00, over 90% of the PPF was crosslinked. The fraction of NVP incorporated into the crosslinked structure increases linearly with the PPF/NVP ratio, with the remainder being unreacted NVP or low molecular poly(*N*-vinyl pyrrolidone), PNVP. PNVP is a water-soluble polymer that was used for decades as a blood-plasma extender and is currently used in various pharmaceutical compositions. PNVP induces only minor storage-related functional changes in organs, and its cytotoxicity is extremely low.[32]

Table II Compressive Strength of the Composites with Fumarate-Based Polyesters

Sample No.	Diol	Catalyst	Peak Load (kg)	Compressive Strength (MPa)	Modulus (MPa)
20	PD	PTSA	23.5 ± 2.7	8.1 ± 0.4	87.4 ± 16.1
14	PD	$TiCl_4$	66.5 ± 3.5	23.1 ± 7.3	580 ± 170
13	PD	$ZnCl_2$	70.2 ± 4.3	24.3 ± 8.7	839 ± 165
11	PD	Ti $(OC_4H_9)_4$	65.4 ± 3.7	22.7 ± 7.8	670 ± 138
17	MPD	$ZnCl_2$	42.5 ± 3.9	14.7 ± 6.3	312 ± 87
26	DMD	$ZnCl_2$	23.8 ± 8.3	8.3 ± 3.5	217 ± 54

Mechanical properties of the cured fumarate-based polyester composites are presented in Table II. From the compressive testing of standardized cylindrical specimens, the lowest tensile properties are shown by the composite prepared with the PTSA catalyzed polyester. This polyester apparently has a diminished number of the available fumarate double bonds for cross-linking in the composite due to saturation reactions (structures **D** and **E**). The composites with the polyesters prepared with the metallic catalysts have a higher number of the available double bonds and better compressive strength and modulus. The composites with MPD or DMD polyesters have lower compression strength than PD composites, as expected due to greater backbone flexibility, as evidenced by the lower T_g of these polymers. It was noted that strength of the aliphatic polyesters is highest when unbranched glycols are used.[28]

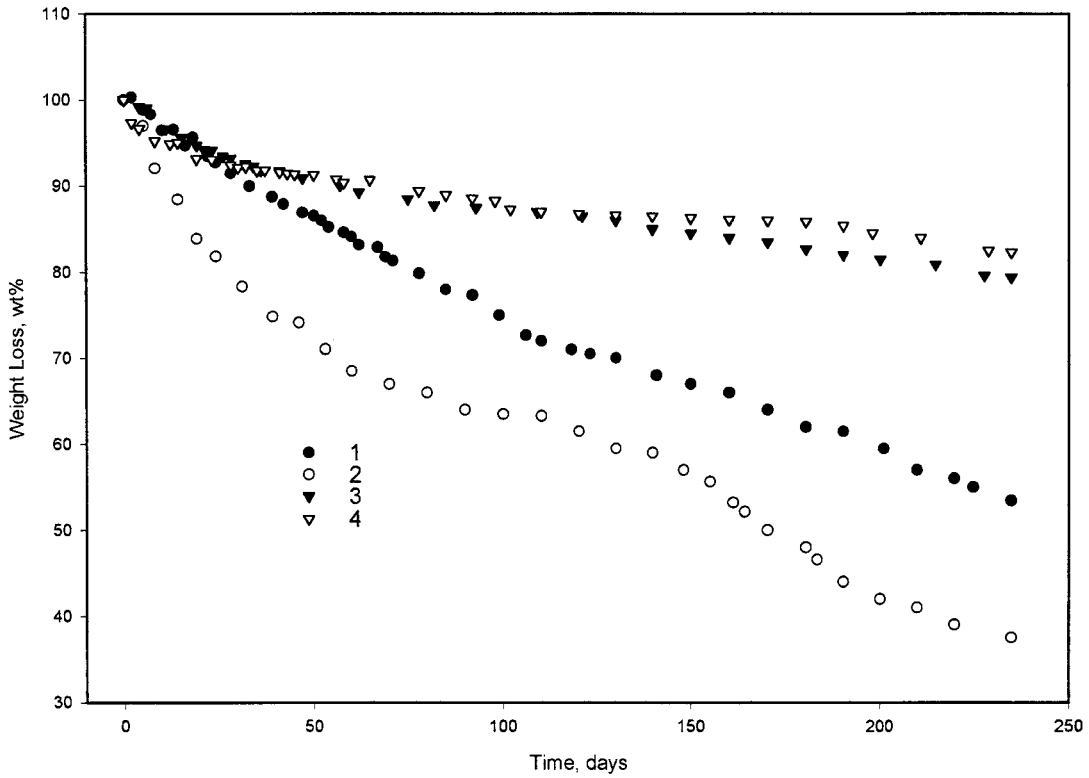


Figure 6 Weight loss of fumarate-based polyesters degraded in phosphate buffered saline: (1) PPF ($ZnCl_2$), (2) PPF (PTSA), (3) MPD, and (4) DMD.

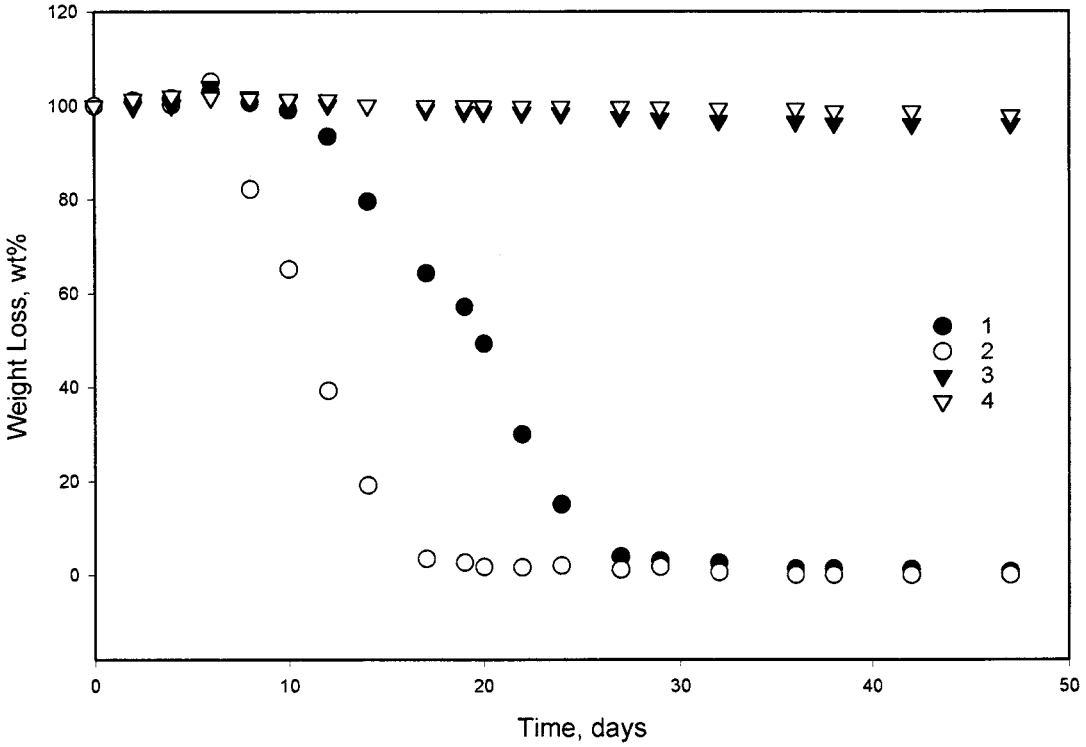


Figure 7 Weight loss of composites with fumarate-based polyesters degraded in phosphate buffered saline: (1) PPF ($ZnCl_2$), (2) PPF (PTSA), (3) MPD, and (4) DMD.

Degradation Studies

The biodegradability of aliphatic polyesters is attributed to their ability to undergo hydrolysis back to their respective monomeric carboxylic acids and diols.[32] Hydrolysis can occur via the ester bond, resulting in the formation of alcohol and carboxylic acid end groups. These monomers, in turn, are shunted to metabolic pathways, where they are enzymatically transformed into carbon dioxide and water.

In vitro demonstration of biodegradation requires experimental conditions mimicking the physiological characteristics of living media, especially constant osmolarity and neutral pH. Thus, 0.13*M* phosphate buffer (pH 7.4) at 37°C was used as *in vitro* medium in order to provide isoosmolarity and to neutralize the generated carboxyl groups without changing the pH of the medium. The degradation rate by hydrolysis of fumarate-based polyesters (Fig. 6), as well as bone cement compositions (Fig. 7), were measured as the mass loss over time of exposure to the buffer solution.

Degradation of PPF prepared in the presence of PTSA starts after about eight days, a few days earlier than PPF catalyzed with $ZnCl_2$ (Fig. 6). Again, the polyesters' structural differences can account for different hydrolytic stability. The rates of degradation measured from the linear weight loss after eight days for PPF (PTSA) and 12 days for PPF ($ZnCl_2$) are 9.3 and 5.9% per day, respectively. More branched polyester (PTSA) chains create more porous structure for water diffusion and hydrolysis. MPD- and DMD-based polyesters have much higher stability due to the more hydrophobic character of their backbones. The presence of substituted diols in the polyester backbone leads to hydrolysis resistance because of the steric hindrance of these diols, which prevent the attack of ester linkages.[28]

Cured composites degrade much slower than unmodified polyesters (Fig. 7). The rates of degradation for first 40 days are 0.8 and 0.3% per day for PPF polyesters prepared with PTSA and $ZnCl_2$, respectively. This is probably associated with the embedding the polymer in filler and the constraining of PVP crosslinking on PPF hydrolysis. The mass loss pattern of the composites with PTSA and $ZnCl_2$ prepared fumarate polyesters is the same as that of uncrosslinked polyesters. The composite with PPF (PTSA) degrades faster than

one with PPF ($ZnCl_2$). Composites with MPD and DMD polyesters lose mass very slowly due to higher stability of the polyesters, resulting from greater hydrophobicity.

CONCLUSIONS

It was shown by applying high-resolution NMR analysis that PPF prepared with PTSA as a catalyst has a rather complex structure of different regiospecificity as a consequence of different modes of addition of 1,2-propanediol and with a decreasing number of double bonds due to side reactions. Our initial experiments indicate that the extent of side reactions, as well as the PPF structure, can be controlled by the choice of catalyst. Polymerization in the presence of a metal containing catalyst, e.g., $ZnCl_2$, which can coordinate with the hydroxy groups of 1,2-propane diol, gives a more regular polymer with a higher content of double bonds than does polymerization using PTSA.

The polyester structure has significant impact on the properties of the bone cement composites prepared by crosslinking the fumarate polyesters with *N*-vinyl pyrrolidone in the presence of an inorganic filler, $CaSO_4 \cdot 2H_2O$, with the addition of a radical initiator, benzoyl peroxide, at ambient temperatures. Maximum compressive strength is achieved when composites are prepared using unbranched PPF having a high content of the double bonds, i.e., as prepared using PD and a metal-containing catalyst. Hydrolytic stability of the cements can be correlated with the hydrophilic–hydrophobic composition of the polyesters.

This work was supported by grants from the DePaul University Research Council and DynaGen, Inc.

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