Hydrolytic Degradation and Diffusion Studies on a Polyphosphate Ester

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ABSTRACT: A polyphosphate ester was synthesized by interfacial polycondensation of bisphenol-A and phenylphosphorodichloridate. Accelerated hydrolytic degradation studies were conducted under alkaline conditions. The effect of concentration of alkali and temperature were monitored. The rate of degradation reached a maximum value at 6 molar sodium hydroxide solution and then reduced. The activation energy for hydrolytic degradation was found to be 45 kcal/mol. Diffusion of alkali into the polymer pellet was studied at various concentrations of alkali and at various temperatures. The rate of diffusion also attained a maximum at $6M$ NaOH and the activation energy for diffusion process was found to be 12 kcal/mol. © 2002 John Wiley & Sons, Inc. J Appl Polym Sci 84: 701–708, 2002; DOI 10.1002/app.10008

Key words: hydrolytic degradation; polyphosphate ester; rate of degradation; rate of diffusion; activation energy

INTRODUCTION

When there are hydrolyzable linkages present in a polymer, as in condensation polymers like polyesters, polyamides, and so forth, the polymers can be degraded by water, which is called *hydrolytic degradation.* Hydrolytic degradation can be catalyzed by acids, alkali, and enzymes. When hydrolytic degradation is catalyzed by enzymes, it is referred to as *biodegradation.* Thus hydrolytically degradable polymers are potentially biodegradable. Hydrolytically degradable polymers and biodegradable polymers have applications in medicine as degradable surgical sutures, controlled drug-delivery systems, and degradable implants.[1–3] Of all the polymers studied for hydrolytic degradation and biodegradation very little work has been reported on polyphosphate esters. Leong[4,5] was the first to report on polyphosphate esters as biodegradable polymers. The first report on the kinetics of hydrolysis of polyphosphate esters was reported by Penczek et al.[6] Polyphosphate esters are also an important class of organophosphorus polymers because of their flame-retardant property.[7–10]

Generally the *in vitro* hydrolytic degradation under physiological conditions (pH 7.4, 37°C) is very slow and takes several days to observe. To facilitate the degradation process, accelerated degradation studies can be done at variable pH (either acidic or alkaline) or at high temperatures. The polymer from bisphenol-A and phenyl phosphorodichloridate (poly–BPA) was previously studied for hydrolytic degradation at pH 12 in phosphate buffer at 37°C. Poly–BPA is currently under consideration as a potential biodegradable polymer for biomedical applications.[5] In this study we report on a detailed investigation of the hydrolytic degradation of poly–BPA under accelerated conditions (alkaline media). We chose an alkaline medium, given that phosphate triester hydrolysis is mainly catalyzed by alkali.[11]
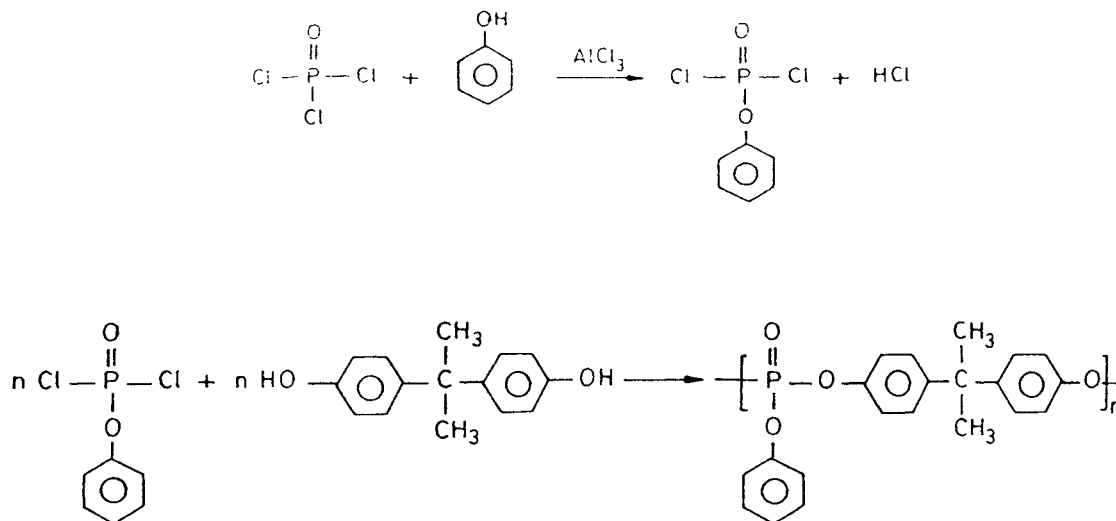
Scheme 1 Synthesis of poly–BPA.

EXPERIMENTAL

Phenylphosphorodichloridate was synthesized from phosphorus oxychloride and phenol as reported earlier.[12] Poly–BPA was synthesized by interfacial polycondensation of bisphenol-A and phenylphosphorodichloridate as already reported[13] (**Scheme 1**). It was characterized by FTIR and ^{1}H-, ^{13}C-, and ^{31}P-NMR spectroscopy. The IR and NMR data were previously reported for this polymer.[14]

Hydrolytic Degradation Studies

About 250 mg of finely powdered polymer was compressed in a die up to a pressure of 5 tons. The pellet dimensions were: diameter, 10 mm; thickness, 2.6 mm. Ten pellets were used for a single experiment. The 10 pellets were placed each in numbered test tubes (125 × 12 mm) with a hole and bulge at the bottom. The test tubes were placed in a circular stainless-steel stand with 10 holes, which was then placed inside a 2-L beaker containing the sodium hydroxide solution. The whole setup was then placed in a thermostat (Fig. 1).

First the thermostat was brought to the desired temperature and then the 2-L beaker containing only the NaOH solution of a particular concentration was kept in the thermostat for 1 h to attain thermal equilibrium. After 1 h the stainless-steel containing the test tubes with the pellets was placed inside the beaker. The sodium hydroxide solution rose into the test tubes through the holes at the bottom of each test tube.

Because the pellets started to float, glass rods were placed on top of the pellets to keep them immersed in the solution. The test tubes were removed, one at a time, after given time intervals and washed with distilled water; placed in 1% HCl solution for about 2 min, and further washed again with distilled water until the washings were neutral to pH paper. Subsequently, the test tubes having the pellets were dried in a vacuum dessicator for about 36 h, after which the final weights of the pellets were recorded. From the difference between their initial and final weights the percentage of weight loss was calculated and plotted against time.

Density Measurements

The density of the polymer pellets was determined based on the Archimedes principle.[15] From the values of the dry weight of the pellet (w_1) and
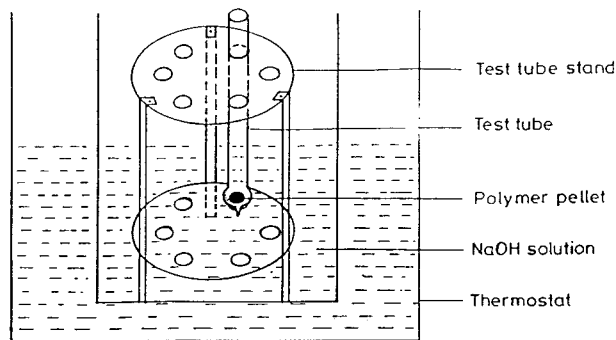

Figure 1 Experimental setup for hydrolytic degradation studies.

the weight of the pellet when immersed in water (w_2), the density of the pellet was calculated from the following equation:

$$D = \frac{w_1}{w_1 - w_2}$$

Diffusion Studies

To study the diffusion of sodium hydroxide into the polymer, a simple thick-walled glass capillary tube (0.2 cm) was used. To pack the capillary with a constant density of polymer column the exact radius of the capillary tube should be known. It was determined by a standard method.

Finely powdered polymer was packed tightly inside the preweighed capillary tube up to half its height and the length (l) of the polymer column was noted. From the final weight of the tube with the polymer, the weight of the polymer (w) was determined. Given that the radius of the capillary tube was already determined, the density of the polymer column in the capillary tube was determined using the equation

$$d = \frac{w}{r^2 l}$$

The density of the polymer column was kept nearly constant at 0.65 ± 0.05 gm/cm^3.

The diffusion experiments were carried out inside an incubator with temperature accuracy of 1°C. The incubator was fitted with a glass door for direct observation of the diffusion process. The sodium hydroxide solution of appropriate concentration was prepared and a few drops of phenolphthalein added to form pink color. For very high concentrations of sodium hydroxide (14M and above) the phenolphthalein was not miscible and thus was not used.

The capillary tube filled with polymer was tied to a scale at its back and placed inside the incubator for about 1 h along with a small beaker containing about 2 ml of NaOH solution. At the end of 1 h the capillary tube was dipped into the alkali solution and was allowed to diffuse into the polymer column (Fig. 2). The diffusing alkali front was readily monitored because of the presence of the pink color or wetting of the polymer column. The distance traveled by the alkali front was noted at regular time intervals from the scale. The distance traveled was plotted with respect to time.
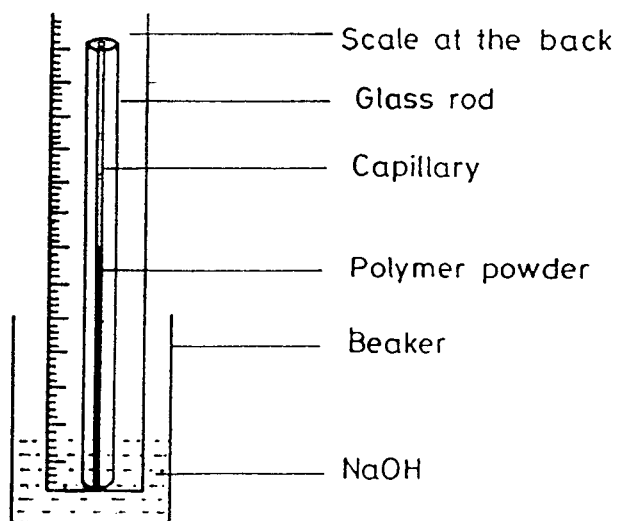

Figure 2   Experimental setup for diffusion studies.

RESULTS AND DISCUSSION

Poly–BPA was synthesized by interfacial polycondensation of phenylphosphorodichloridate and bisphenol-A in the presence a phase-transfer catalyst. The polymer was characterized by FTIR and ^{1}H-, ^{13}C-, and ^{31}P-NMR spectroscopy. The molecular weight was found to be 2928 by endgroup analysis using ^{31}P-NMR spectroscopy.

Hydrolytic Degradation Studies

We studied the effect of concentration of alkaline media and the effect of temperature on the hydrolytic degradation of poly–BPA. The hydrolytic degradation of the polymer in different concentrations of sodium hydroxide (2, 4, 6, 8, and 10M NaOH at 37°C) was performed. The percentage weight loss of the polymer pellets at different time intervals was calculated. In a 2M NaOH solution there was only 0.9% weight loss in 340 min. About 5–7% weight loss was observed at higher concentrations. The mean of the weight loss in two experiments was further least-square fitted and linear plots could be drawn with respect to time in all the concentrations, except in 2M. Typical plots of weight loss versus time plots for 6 and 10M NaOH are shown in Figures 3 and 4, respectively. The slopes of the linear plots give the rate of degradation. The rate of degradation thus obtained was plotted against concentration of NaOH (Fig. 5). Figure 5 shows that the rate of degradation initially increases with concentration up to 6M; thereafter, the rate decreases for 8 and 10M solutions. Thus the order of degradation is as
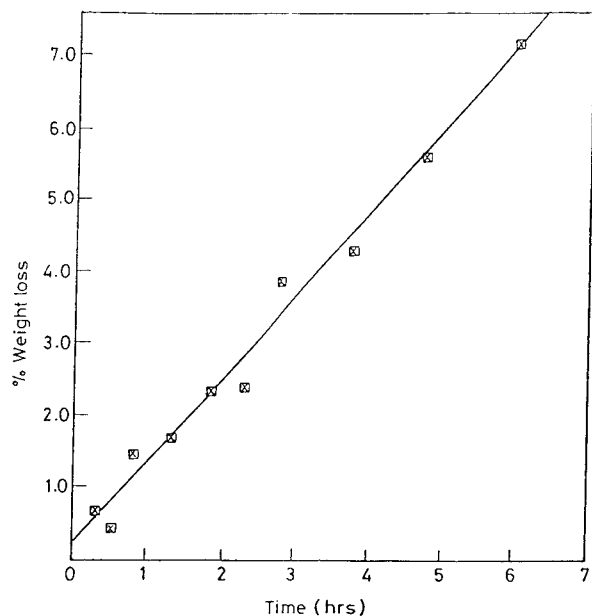
Figure 3 Weight loss versus time in 6M NaOH.

follows: 6M > 8M > 10M > 4M > 2M. One would expect that the rate of degradation would increase linearly with concentration of alkali solution, although this is not observed. This indicates that there could be other factors, apart from concentration of alkali, which affect the rate of degradation. One factor might be diffusion of alkali into the pellet, given that this is a heterogeneous reaction. Thus, the role of diffusion has to be further studied.
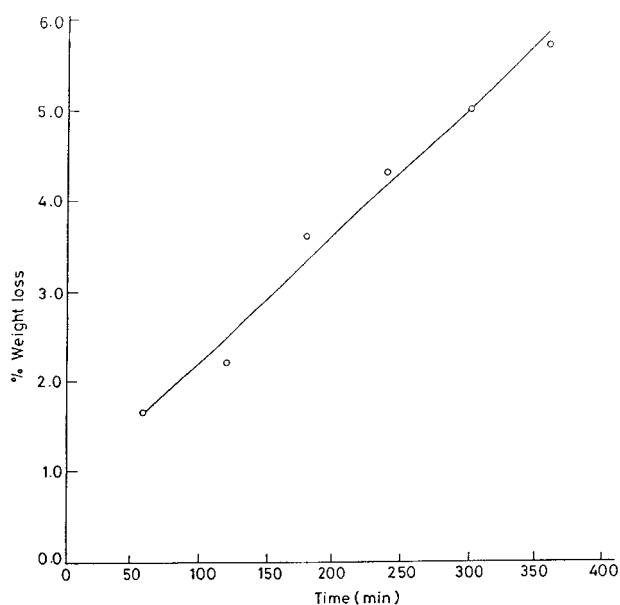

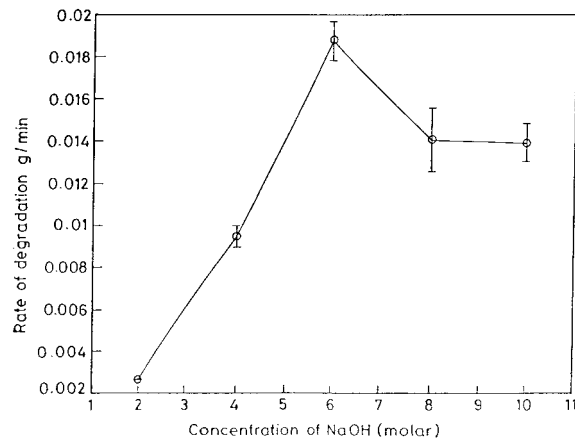**Figure 4** Weight loss versus time in 10M NaOH.

Figure 5 Rate of degradation versus concentration of NaOH.

The hydrolytic degradation of the polymer was carried out in different temperatures, that is, 30, 35, 37, and 40°C in 6M NaOH. The weight loss versus time plots for different temperatures are shown in Figure 6. As the temperature increases the rate of degradation increases, thus obeying Arrhenius behavior. The activation energy for the degradation reaction was calculated using the Arrhenius equation
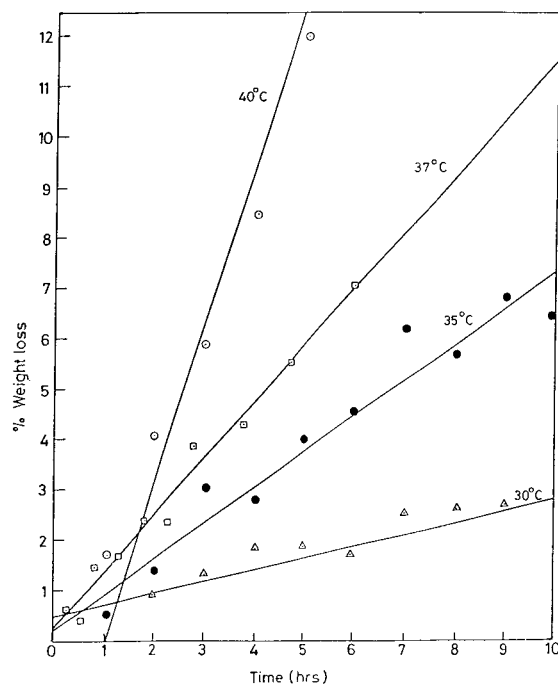
$$K = Ae^{-E_a/RT}$$

Figure 6 Plot of weight loss versus time at different temperatures.

where the rate constant K was obtained from the slopes of the linear plots for different temperatures (Fig. 6). On plotting log K versus $1/T$, a linear plot was obtained and from the slope of this linear plot the activation energy was calculated. The activation energy was found to be 45 kcal/mol. There are no reports in the literature on the determination of activation energy for hydrolytic degradation of any phosphate polymer. However, for analogous low molecular weight triphenyl phosphate, the activation energy for hydrolysis in an alkaline medium was found to be 45 kcal/mol.[16] Thus, the activation energy obtained for the polymer matches that obtained for the low molecular weight compound, indicating a similar process of degradation in both systems.

To find out whether there are any changes in the density of the pellets after hydrolysis, in one of the hydrolysis experiments the densities of the polymer pellets were determined before and after hydrolysis. It was found that the density of the pellets decreases after hydrolysis. The decrease in density varies from 1.2% at the end of a 3-h exposure to 10.6% at the end of a 10-h exposure to alkaline media. If the degradation occurs only at the pellet–alkali interface there should not be any decrease in density, given that, as the mass of the pellet decreases because of degradation, the volume of the pellet would also decrease proportionally. Actually, there is a decrease in density, which shows that the weight of the pellet de-
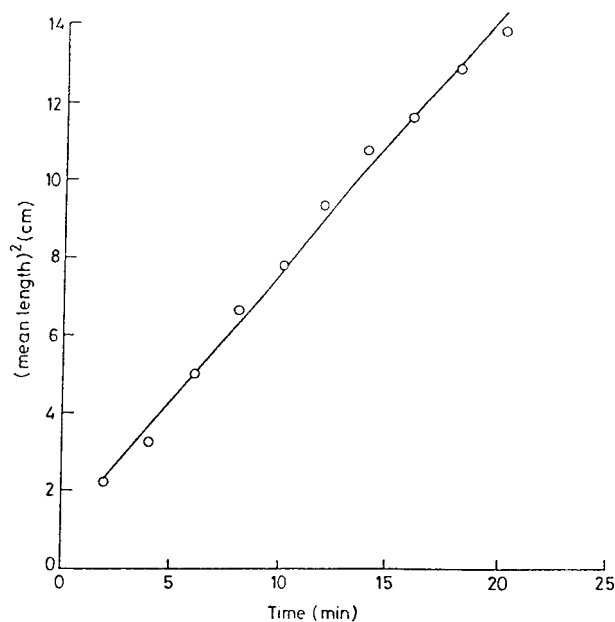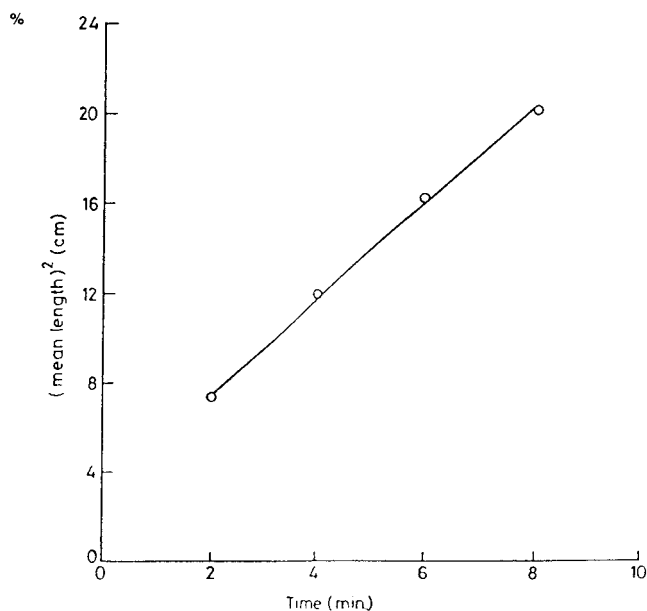

Figure 8 Plot of (mean length)^2 versus time in $6M$ NaOH.

creases, although the decrease in the volume of the pellet is not proportional. So we assume that bulk degradation also occurs along with surface degradation.

Diffusion Studies

The density measurements of the pellets indicate that bulk degradation also occurs along with surface degradation. Bulk degradation can occur only by the diffusion of alkali solution into the pellet. Thus diffusion also plays an important role in the hydrolysis reaction. To study the role of diffusion, the following studies were carried out.

Diffusion of NaOH into the polymer was performed at different concentrations of NaOH and also at different temperatures. Five to six runs were done for each experiment. The mean length traveled by the alkali was determined. When the mean length was plotted against time a curved plot was obtained, although no parameters could be obtained from this curved plot. Diffusion processes obey the square law[17]

$$l^2 = mt + c$$

where l is the mean length, t is time, and c is a constant. When l^2 is plotted against time a linear plot is obtained. The slope (m) of this plot gives a measure of the rate of degradation.
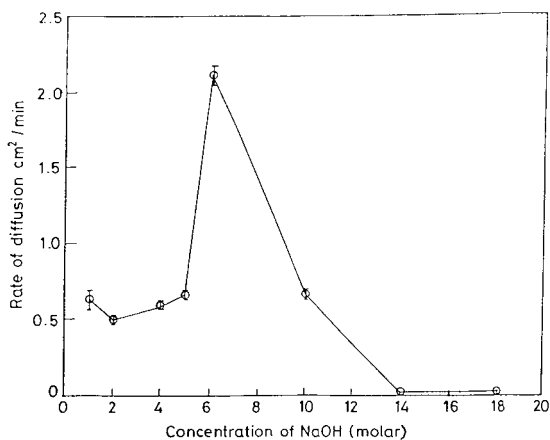

Figure 7 Plot of (mean length)^2 versus time in $5M$ NaOH.

Figure 9 Rate of diffusion versus concentration of NaOH.

the linear plots were determined and plotted against the concentration of NaOH, which is shown in Figure 9. As the concentration is increased the rate of diffusion increases, reaches a maximum at $6M$ concentration, and then decreases. It is to be noted here that, similar to the maximum rate of degradation occurring at $6M$ NaOH (Fig. 5), the maximum rate of diffusion also occurs at $6M$ (Fig. 9). Thus, it appears that diffusion of alkali in the polymer also plays an important role in controlling the hydrolytic degradation. It is known that diffusion depends on viscosity of the solution, which in turn depends on concentration of the solution. At low concentrations of alkali, the viscosity of the solution is low and hence the rate of diffusion should be high. As the concentration is increased the viscosity increases and the rate of diffusion should decrease. Thus, a linear plot should have been obtained, but which is not observed, suggesting that viscosity is not the only factor. The other factor could be the hydrolysis reaction rate because the reaction can

The diffusion experiments were carried out at different concentrations of NaOH (1, 2, 4, 5, 6, 10, 14, and 18M) at 30°C. Typical plots of l^2 versus time are shown in Figures 7 and 8. The slopes of
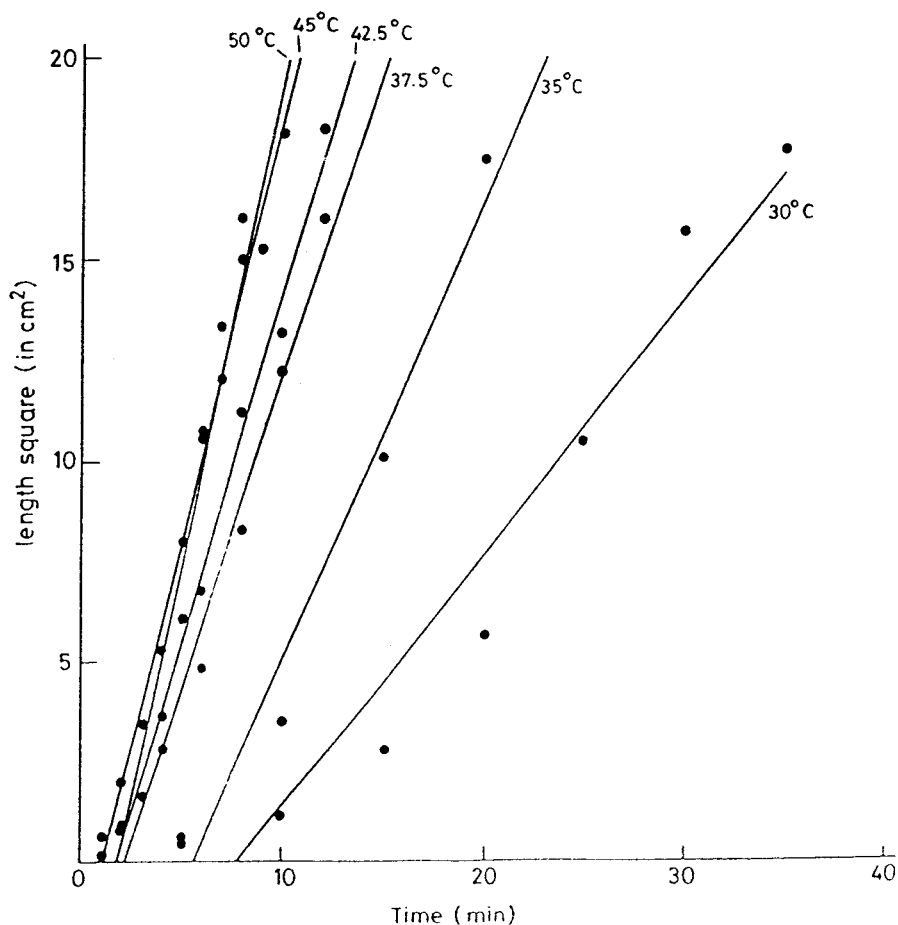

Figure 10 Temperature effect on diffusion.

also occur along with diffusion. Given that a similar trend is seen in both the hydrolysis reaction and the diffusion process, it appears that diffusion and the hydrolytic reaction are coupled so that the rate of diffusion depends on both the viscosity and the hydrolytic reaction rate. Thus, in Figure 9 at low concentrations, the hydrolytic reaction predominates and the rate of diffusion is less. This trend is seen up to 6M. After 6M the viscosity predominates and thus the rate of diffusion decreases as the viscosity increases.

To negate the role of capillary action in the diffusion process, we carried out diffusion experiments with NaOH (5.38M) and NaCl (5.32M) solutions of the same density. Whereas the NaOH solution diffused up the polymer column, there was no diffusion with NaCl solution. If there were capillary action, the NaCl solution should also have diffused, although only the NaOH solution diffused. This shows that there is no capillary action and the diffusion process mainly results from the reaction between NaOH and the polymer. Thus this diffusion process may be termed as *reactive diffusion.*

To determine the activation energy for this diffusion process, diffusion experiments were carried out at six different temperatures (30, 35, 37.5, 42.5, 45, and 50°C) in 1M NaOH solution. The plots of (mean length)^2 versus time at all these temperatures are shown in Figure 10. The slopes give the rate of diffusion. As the temperature increases the rate of diffusion also increases. Because the rate of diffusion, as discussed earlier, depends on the hydrolysis reaction rate, as the temperature is increased the hydrolysis reaction rate increases and thus the rate of diffusion increases with temperature. The logarithm of the above plots were plotted against 1/T. A straight line was obtained, obeying the Arrhenius equation. From the slope of this straight line the activation energy was calculated and found to be 12 kcal/mol.

The density measurements of the polymer pellets before and after hydrolysis clearly showed that there is bulk degradation, which can occur only by diffusion of alkali into the polymer pellet. Diffusion experiments have shown that at higher concentrations the rate of diffusion is less, which explains the trend obtained in the hydrolytic degradation experiments in which the rate of hydrolysis decreases at higher concentrations (Fig. 5).

For the reactive diffusion, we obtained an activation energy of 12 kcal/mol, whereas for the hydrolytic degradation we obtained an activation energy of 45 kcal/mol. Thus the diffusion process
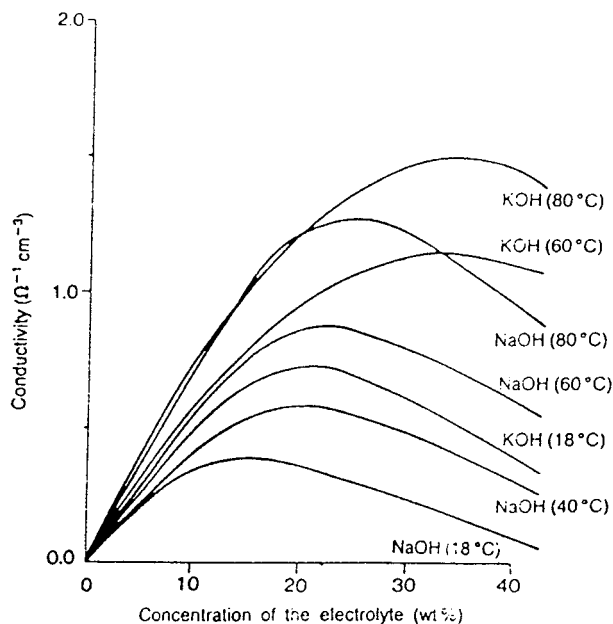

Figure 11 Plots of conductance maxima for NaOH and KOH (taken from Ref. 18).

is faster than the hydrolytic degradation and shows that, first, NaOH diffuses into the pellet followed by the hydrolysis of the polymer. Hydrolysis of the polymer is the rate-controlling step in this process.

Looking for other factors that can explain why we obtain a maximum hydrolytic degradation at 6M and also a maximum rate of diffusion at 6M NaOH, we can ascribe it to the maximum number of hydroxyl ions in the NaOH solutions. In electrochemistry it is known that the conductance maximum occurs at 5.5M (which is close to 6M) for NaOH at 40°C (Fig. 11),[18] which means that the maximum number of Na$^+$ and OH$^-$ ions are present at this concentration. Hence, the hydrolytic reaction rate may be higher at this concentration.

CONCLUSIONS

Poly–BPA was synthesized by interfacial polycondensation of phenylphosphorodichloridate and bisphenol-A and its hydrolytic degradation was studied. The maximum rate of hydrolytic degradation was observed in a 6M NaOH solution. The activation energy for the degradation process was found to be 45 kcal/mol. Density measurements of the polymer pellets showed that bulk degradation occurs along with surface degradation. Diffusion studies show that the maximum rate of diffusion

also occurs in a 6*M* NaOH solution. The activation energy for the diffusion process was found to be 12 kcal/mol.

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