

Ethyl-4-(Dimethylamino) Benzoate Initiation of the Spontaneous Polymerization of Aqueous Acidic Adhesive Formulations in the Presence of a Base

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ABSTRACT: This study indicated that the spontaneous polymerization of an aqueous acidic dental adhesive system containing ethyl-4-(dimethylamino) benzoate (4E) could be activated by various bases. The adhesive was prepared with a monomer mixture of bis[2-(methacryloyloxy)ethyl] phosphate (2MP) and 2-hydroxyethyl methacrylate (HEMA). Various amounts of base [hydroxyapatite (HAP) and its analogues, e.g., Ca(OH)₂, NaOH, and calcium carbonate] were added. Real-time Fourier transform infrared-attenuated total reflectance spectroscopy was used to monitor the polymerization process. The pH and buffer capacity affected the degree of conversion, and the polymerization rate and induction period were evaluated. The optimal conditions for the pH of this system was between 1.0 and 1.8, and HAP had the best performance on polymerization because of its excellent buffer capacity. The mechanism for the spontaneous polymerization of the 2MP/HEMA adhesive system was proposed with 4E as an initiator. © 2013 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* 130: 2698–2706, 2013

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INTRODUCTION

The vast majority of contemporary dental adhesives are acrylate-based resins that rely on photo-initiated polymerization to cure.^{1–3} Each prevalent photo-initiation system is composed of a photosensitizer, typically, camphorquinone (CQ), and a hydrogen-donating coinitiator, usually a tertiary aromatic amine, such as ethyl-4-(dimethylamino) benzoate (4E).^{3–6} The advantage of light curing is obvious; it is fast and controllable.⁷ Under certain circumstances, however, light curing alone cannot ensure a maximal degree of polymerization of the resin. For example, it is sometimes very difficult to position the curing light at the right location and angle it for cavities in the posterior teeth; this could result in inadequate or uneven light exposure. In addition, the penetration of light irradiation into deep cavities and endodontic preparations such as in a root canal is especially poor as well. An incomplete conversion of monomeric species would not only reduce the mechanical strength of the adhesion⁸ but could also pose a cytotoxic threat to oral tissues.⁹ Situations like these call for dual-curing (both light- and chemical-curing) adhesives.

Commercial dual-curing adhesives all feature a two-component system, wherein a resin monomer and chemical activator are

stored separately out of storage stability considerations. Common chemical activators include organic peroxide and sodium benzene sulfonate, the former of which undergoes cleavage at the peroxide O-O bond and generates free radicals,¹⁰ whereas the latter produces free radicals in an acidic environment.¹¹ Upon thorough mixing of the two components, the dual-curing adhesive must be applied immediately to the tooth-bonding substrate; otherwise, it will set prematurely. This adds to operational inconvenience and technique sensitivity. The issue of short working time could be solved, in theory, if the chemical activator is donated by the teeth instead.

We recently discovered an unexpected tooth-originated activator. It was when we explored the properties of a model self-etching adhesive containing an acidic acrylic monomer bis[2-(methacryloyloxy)ethyl] phosphate (2MP), a functional monomer 2-hydroxyethyl methacrylate (HEMA), and the classic CQ/4E photoinitiator that we found that the resin solidified in the absence of light after the addition of a small amount of hydroxyapatite (HAP), a calcium phosphate hydroxide salt abundant in enamel and dentin. After repeated experiments to rule out the possibility of accidental light exposure, we turned to the

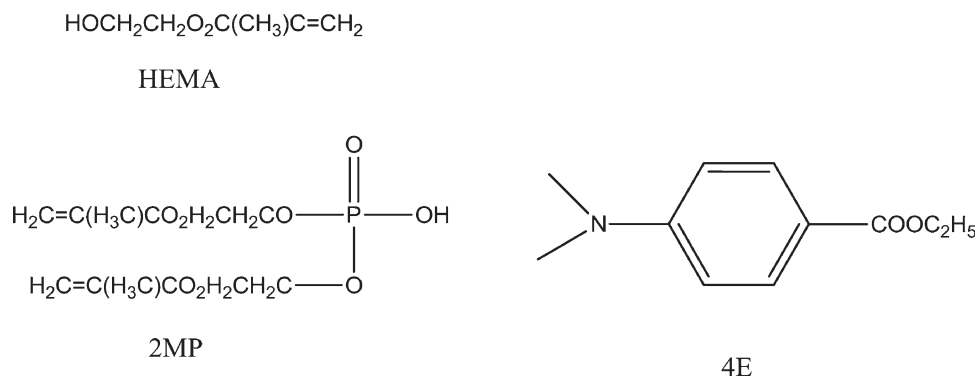


Figure 1. Chemical structure of HEMA, 2MP, and 4E.

literature to determine if a similar phenomenon had been observed before. Indeed, it was reported decades ago^{12–14} that the spontaneous polymerization of acrylic monomers could be triggered by a combination of carboxylic acids (in our case, the acidic phosphate functional group) and aromatic amines such as *n*-phenyl glycine (NPG; in our case, 4E). The mechanism was uncertain but was speculated to involve the formation of a transient salt or complex between the acid and amine, which is unstable and decomposes into initiating species.¹⁵

Nevertheless, the proposed mechanism in the literature could not explain why no additional activator was needed, whereas HAP was necessary in our system despite the similarity between the two. As such, it was the objective of this study to investigate HAP's role in kicking off the spontaneous polymerization of a 2MP-containing model adhesive (2MP/HEMA). We examined the polymerization behavior *in situ*, including the rate of polymerization (R_p), degree of conversion (DC), and induction period (IP) when various amounts of HAP and HAP analogues [including various bases, e.g., $\text{Ca}(\text{OH})_2$, NaOH, and calcium carbonate (CaCO_3)] were introduced into the HEMA/2MP/water/4E system. The photosensitizer CQ was removed from the formulation to eliminate the interference of light-induced polymerization all together. On the basis of the change in 2MP/HEMA's polymerization behavior with respect to the pH shift and alternative cations and anions, we attempted to gain a better understanding of the HAP-activated spontaneous polymerization of the model adhesive.

EXPERIMENTAL

Materials

2MP, HEMA, 4E, and hydroxyl apatite (HAP) were purchased from Sigma-Aldrich (Milwaukee, WI). Deuterium oxide (D_2O) was purchased from Cambridge Isotope Laboratories, Inc. (Andover, MA). Calcium hydroxide [$\text{Ca}(\text{OH})_2$], sodium hydroxide (NaOH), and CaCO_3 were purchased from Acros (Morris Plains, NJ). All chemicals were used as received. The chemical structures of HEMA, 2MP, and 4E are shown in Figure 1.

Sample Preparation

Adhesives consisting of 40 wt % HEMA, 40 wt % 2MP, and 20 wt % D_2O were prepared by the addition of calculated amounts of the chemicals into glass vials followed by thorough mixing with a vortex. After homogeneity was reached, the aromatic

amine 4E was introduced into each mixture at a fixed concentration of 0.088 mmol/g. Subsequently, various quantities of the activator HAP were added to individual vials to selected concentrations of 0.5, 1, 2, 4, 6, and 8 wt %, respectively, with regard to the weight of the 4E-containing adhesives. Samples activated by the HAP analogues $\text{Ca}(\text{OH})_2$, NaOH, and CaCO_3 were prepared in the same pattern. All of the samples were prepared at room temperature. The HAP-solvated and HAP-analogue-solvated adhesives were bath-sonicated for 1–2 min to ensure an even dispersion of activators. Immediately after the good mixing of all of the components, Fourier transform infrared (FTIR)–attenuated total reflectance (ATR) measurements were performed.

Real-Time FTIR–ATR Spectroscopy

The spontaneous polymerization of each prepared adhesive was monitored in real time with an FTIR spectrometer (Spectrum One, PerkinElmer, Waltham, MA) equipped with an ATR attachment in the absence of light. Briefly, a few drops of the sample solution were placed on the ATR diamond crystal top plate, and the top surface was covered by a $22 \times 22 \times 0.25$ mm³ polyester film (Fisher Scientific, Pittsburg, PA). A black polyester sheet was then used to cover the entire ATR unit so that any light interference could be avoided during polymerization. The spectra were recorded at a resolution of 4 cm^{-1} in the wave-number range between 700 and 4000 cm^{-1} . Time-based spectrum acquisition software (Spectrum TimeBase, PerkinElmer) was used to automatically acquire the spectra at time intervals of 10 min for a total duration of 24 h. The measurement was conducted at room temperature under an ambient atmosphere.

Determination of DC, R_p , and IP

Two characteristic bands at 1637 cm^{-1} (the stretching of the methacrylate double bond $\text{C}=\text{C}$) and 1450 cm^{-1} (the deformation of CH_3 , as an internal standard) were used to calculate the DC of polymerization. The intensities of these two bands were integrated on the basis of the band-height methodology, and the change in the band ratio (BR) profile with $1637 \text{ cm}^{-1}/1450 \text{ cm}^{-1}$ was monitored. The DC was calculated by the following equation:¹⁶

$$\text{DC}_t(\%) = (1 - \text{BR}_t/\text{BR}_0) \times 100 \quad (1)$$

where the subscripts 0 and t represent the initial stage and intermediate time point t of the polymerization, respectively. R_p

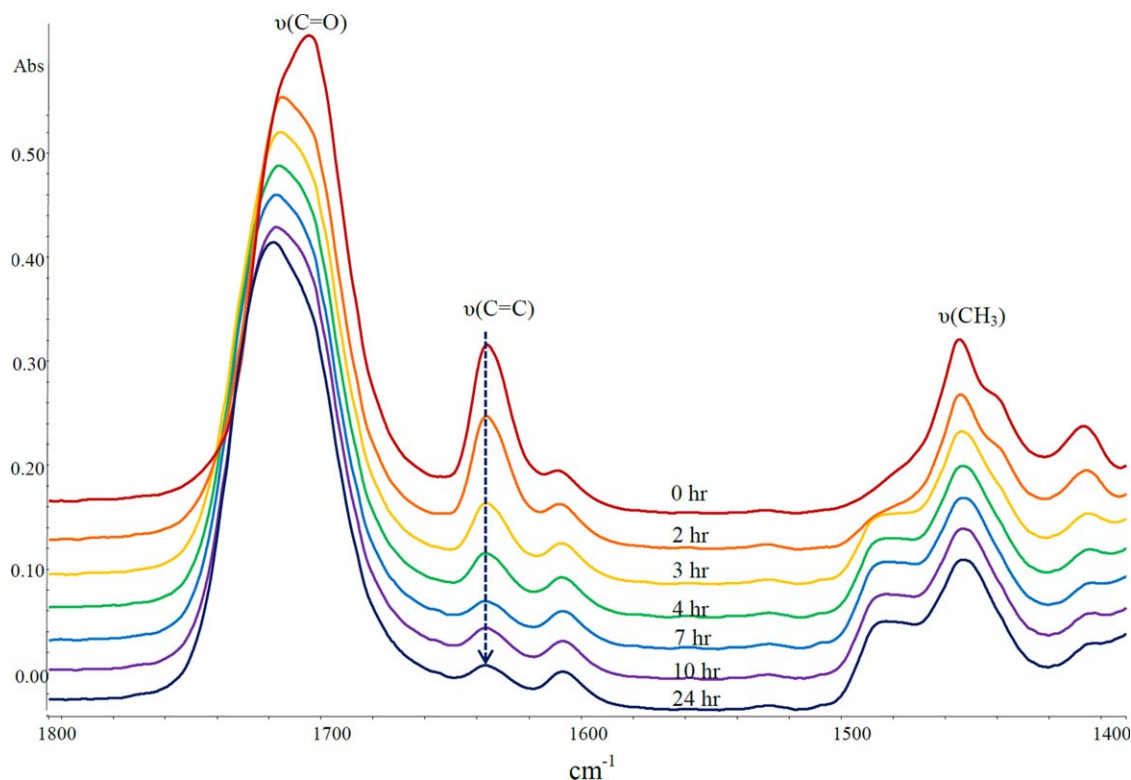


Figure 2. Typical time-resolved FTIR spectra in the region of 1800–1400 cm^{-1} for the spontaneous polymerization of the HEMA/2MP system at 0-, 2-, 3-, 4-, 7-, 10-, and 24-h intervals [4E content = 0.088 mmol/g, water content = 20 wt %, $\text{Ca}(\text{OH})_2$ content = 4 wt %]. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

was calculated with the maximum slope of the linear region of DC versus time and was simulated by least squares linear fitting. IP of the polymerization was determined as the time interval between the starting point of the IR spectral collection and the point that the DC of the adhesive significantly increased.

pH Measurement

The initial pH of each HAP- or HAP-analogue-containing adhesive was measured with a pH meter (Accumet Excel XL15, Fisher Scientific). The pH meter was calibrated with three standard buffer solutions with pHs of 2.00, 4.00, and 7.00, respectively.

RESULTS AND DISCUSSION

The HEMA/2MP system used in this study was a model adhesive referred to as a self-etching adhesive in dentistry. Although HEMA's primary purpose was to help solvate 2MP and decrease the viscosity and increase the hydrophilicity of the formulation, the acidic monomer 2MP functioned to etch dental hard tissues. That is, 2MP was able to dissolve the HAP mineral in enamel and dentin through acid–base reactions. Likewise, when the pure HAP powder was added to the HEMA/2MP model adhesive in our study, the powder was dissolved, and the solution turned clear. Therefore, we speculated that the pH change caused by the neutralization capacity of HAP played a central role in the facilitation of polymerization. Other than pH change, another important characteristic of the HAP-solvated solution was that it resulted in a phosphate-buffered system,

and the buffering effect may have influenced the polymerization behavior as well. Finally, we also examined whether the nature of the cation asserted any effect. With these in mind, we did comparative studies with bases similar to HAP, that is, $\text{Ca}(\text{OH})_2$, NaOH, and CaCO_3 , and the results could help answer these questions.

Time-resolved FTIR spectroscopy is a widely used technique for monitoring the transformation of monomeric species during polymerization reactions. Representative time-resolved IR spectra in the wave-number region 1400–1800 cm^{-1} during the spontaneous polymerization of the 2MP/HEMA system [with the presence of 4 wt % $\text{Ca}(\text{OH})_2$] are shown in Figure 2. The IR bands of interest for our resin system included that at 1637 cm^{-1} , which was attributed to the stretching mode of the C=C double bond, and that at 1450 cm^{-1} , which was assigned to CH_3 deformation. As the polymerization proceeded, the intensity of the former band decreased; this reflected the disappearance of the 2MP and HEMA species, whereas that of the latter remained unchanged (Figure 2). Thus, the band at 1450 cm^{-1} was selected as an internal standard, and the ratio of the band intensities between 1637 and 1450 cm^{-1} was used to gauge DC.

The 3D plots of DC as a function of the time and pH for the four bases, including HAP, $\text{Ca}(\text{OH})_2$, NaOH, and CaCO_3 , are given in Figure 3(a–d), and detailed information regarding the final DC, R_p , and IP values of each formulation is summarized in Table I. As shown in Figure 3(a), the formulation

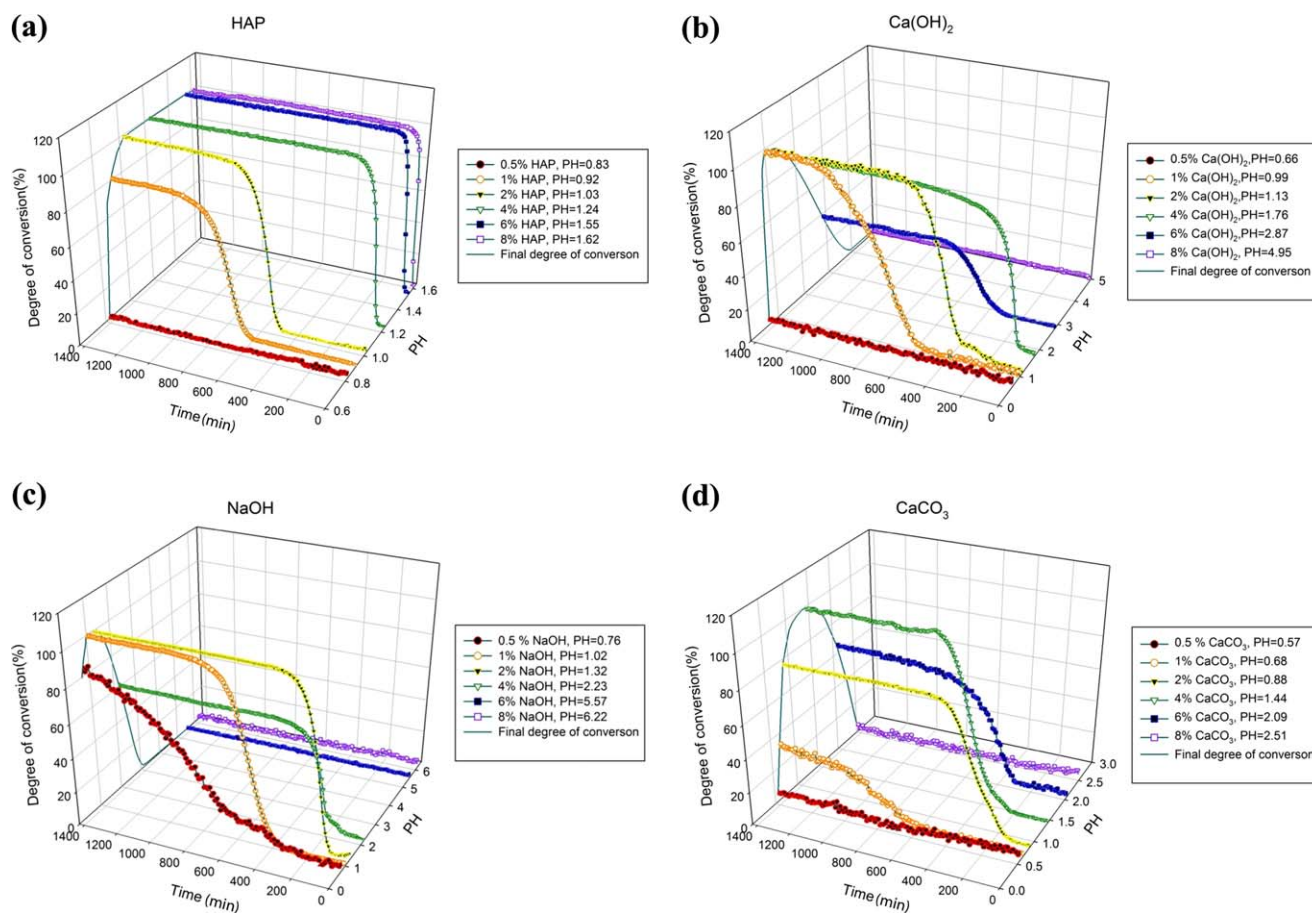


Figure 3. 3-D plot of DC of the HEMA/2MP system with the addition of (a) HAP varied from 0.5 to 8 wt %, (b) Ca(OH)₂ varied from 0.5 to 8 wt %, (c) NaOH varied from 0.5 to 8 wt %, and (d) CaCO₃ varied from 0.5 to 8 wt %. (4E content = 0.088 mmol/g, water content = 20 wt %). The x axis represents the time course, the y axis is the initial pH of the adhesive system, and the z axis represents DC of the 2MP/HEMA adhesive system. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

containing 0.5 wt % HAP (pH 0.83) underwent no polymerization within the scope of the experiment. Upon the addition of 1 wt % HAP to the HEMA/2MP/4E/D₂O formulation (the pH increased to 0.93), the spontaneous polymerization took place with an IP of 600 min, and the maximum DC reached 80.8% at 1000 min. As the incorporated HAP content increased to 2 wt % (the pH increased to 1.03), the final DC increased to 98.9%; this value leveled off to 99.0, 99.1, and 99.4% with the addition of 4 wt % (pH 1.24), 6 wt % (pH 1.55), and 8 wt % HAP (pH 1.62), respectively. The incorporation of HAP at levels higher than 8 wt % was not possible because of the solubility limit of HAP in the adhesive system studied. These results suggest that the nearly complete conversion of double bonds could be achieved with the incorporation of only 2 wt % HAP in this adhesive system. In addition, it was also clear that the increase in the amount of HAP facilitated the polymerization process, as indicated by the decrease in IP and the increase in R_p (Table I).

Knowing that the pH change induced by HAP was limited by its low solubility, we tried a stronger base, Ca(OH)₂, to expand the range of pH while not introducing a different cation; this allowed us to see whether increasing the pH was always

beneficial to the spontaneous polymerization. As shown in Figure 3(b), similar to the case of HAP, the spontaneous polymerization did not occur with 0.5 wt % Ca(OH)₂ (pH 0.66). Upon the addition of 1 wt % Ca(OH)₂ (pH 0.99) and 2 wt % Ca(OH)₂ (pH 1.13), the polymerization proceeded and reached a very high DC around 98%. When more Ca(OH)₂ was added, however, the final DC started to fall as the pH continued to increase [Figure 3(b)]. The incorporation of the highest Ca(OH)₂ content (8 wt %) rendered a pH of 4.95, under which circumstance no polymerization was observed. In comparison to the final DC, the change of R_p with respect to increasing pH exhibited a similar up-and-down pattern with some minor discrepancy; the peak R_p (0.65%/min) was observed at 4 wt % Ca(OH)₂ at pH 1.76, at which point the final DC decreased to 87.6%. Additionally, the change of IP matched R_p very well, as a longer IP was recorded for the reactions with a slower R_p .

To test whether the Ca²⁺ moiety played a role in the spontaneous polymerization, NaOH was used to activate the polymerization. The changes in DC and R_p [Figure 3(c)] showed very similar trends to those of Ca(OH)₂. The polymerization proceeded at a very low R_p (0.087%/min) with 0.5 wt % NaOH

Table I. pH, DC, R_p , and IP Values of the HEMA/2MP/4E/D₂O Adhesive Systems with the Addition of Various Bases

Base content	pH	DC (%)	R_p (%/min)	IP (min)
0.5% HAP	0.83	0	0	N/A
1.0% HAP	0.92	80.8	0.35	590
2.0% HAP	1.03	98.9	0.58	480
4.0% HAP	1.16	99.0	1.20	160
6.0% HAP	1.55	99.1	1.83	20
8.0% HAP	1.62	99.4	2.40	10
0.5% Ca(OH) ₂	0.66	0	0	N/A
1.0% Ca(OH) ₂	0.99	98.0	0.26	460
2.0% Ca(OH) ₂	1.13	97.6	0.43	160
4.0% Ca(OH) ₂	1.76	87.6	0.60	20
6.0% Ca(OH) ₂	2.87	38.5	0.17	280
8.0% Ca(OH) ₂	4.95	0	0	N/A
0.5% NaOH	0.76	84.3	0.09	380
1.0% NaOH	1.02	99.6	0.33	350
2.0% NaOH	1.32	99.3	0.64	330
4.0% NaOH	2.23	70.4	0.38	370
6.0% NaOH	5.57	0	0	N/A
8.0% NaOH	6.22	0	0	N/A
0.5% CaCO ₃	0.57	0	0	N/A
1.0% CaCO ₃	0.68	32.3	0.06	620
2.0% CaCO ₃	0.88	70.0	0.23	480
4.0% CaCO ₃	1.44	98.9	0.35	130
6.0% CaCO ₃	2.09	64.0	0.16	280
8.0% CaCO ₃	2.51	0	0	N/A

N/A = not applicable.

added for a pH of 0.76, and its final DC reached 84.3% within 24 h. The highest R_p , maximum DC, and shortest IP occurred at pH 1.32 when 2 wt % NaOH was incorporated into the 2MP/HEMA adhesive system. The spontaneous polymerization was not observed with NaOH contents as high as 6 wt %; this increased the pH to 5.76. NaOH exhibited a similar effect as Ca(OH)₂ did on the spontaneous polymerization; this indicated that the role of the Ca²⁺ moiety was not critical in this polymerization process.

Considering that the HAP mineral in human teeth is substituted by a trace amount of CO₃²⁻, we investigated whether CO₃²⁻ had any influence on the polymerization with CaCO₃ as the activator. As shown in Figure 3(d) and Table I, the trends of DC, R_p , and IP with respect to the increase in the CaCO₃ content followed the same pattern as those in the cases of Ca(OH)₂ and NaOH. At a low pH of 0.57 (0.5 wt % CaCO₃), there was no polymerization reaction. Polymerization took place when the pH was increased to 0.68 by 1 wt % CaCO₃ with the final DC at 30%. The final DC improved to about 80% as the pH was increased to 0.88 (2 wt % CaCO₃), and finally reached maximum at almost 100% with a pH of 1.44 (4 wt % CaCO₃). After this pH was passed, the final DC declined to about 65% at pH 2.05 (6 wt % CaCO₃); this was followed by a sharp decrease to

almost 0% when the pH was further increased to 2.5 (8 wt % CaCO₃).

As indicated from Figure 3(a–d), the pH had a remarkable effect on the spontaneous polymerization. The previous results also suggest that there was a range of preferred pH for the polymerization instead of always a preferred higher pH. The addition of these four bases led to the increase of the pH and thus resulted in a change in the polymerization process. This effect was demonstrated by the DC versus pH plot, which was generated by the cutting of a plane of X-axis = 1430 min on a three-dimensional (3-D) plot of each base shown in the y - z plane of Figure 3(a–d). Also, as a comparison, the plots of R_p versus pH for different bases are presented in Figure 4. This indicated that the spontaneous polymerization was greatly dependent on the pH value (adjusted by the addition of a base) of the aqueous HEMA/2MP/4E system. In general, the increases in DC and R_p were observed as the content of bases increased until the optimum pH value was reached; then, DC and R_p decreased as the pH increased through the incorporation of a higher content of bases in the formulation. The detailed information obtained from the results showed that the high DC and R_p were observed within the pH range of approximately 1.0–1.8. Particularly, at pHs between 1.4 and 1.7, DC and R_p both reached the maximum value regardless of the bases used. As the pH increased from 2.0 to 5.0, the polymerization reaction was decreased, and this led to a low DC and R_p . In addition, at very low pH (<0.5, before the addition of the base) and high pH (>5.0), the spontaneous polymerization did not proceed at all on the basis of our results.

The existence of such a preferred pH range was obviously the reason why the spontaneous polymerization of the aqueous HEMA/2MP/4E adhesive system had to be activated by the addition of bases such as HAP. The questions were (1) why was the pH so critical and (2) why was such a pH dependency never reported before even for systems with very similar components (i.e., acrylic monomer, acid, and aromatic amine)?^{13,14}

To answer the first question, we hereby propose an initiation mechanism of 4E based upon the following rationale. First of all, our experimental results show that the spontaneous polymerization did not occur at pH values too low; this inferred that a high concentration of H⁺ may have been adverse to the generation of initiating free radicals. Second, the polymerization did not proceed at pH values too high, either; this indicated that an acidic species played a critical role in the initiation step as well. Third, the cation of the base did not affect the R_p or DC; this suggested that the cation should not be included in the mechanism. In reference to an initiation mechanism proposed by Farahani et al.^{13,14} with regard to a similar aromatic amine NPG, our mechanism of 4E initiation is illustrated as follows:

In the proposed mechanism, shown in Scheme 1, the monomer 2MP reacts with the aromatic amine 4E to form a complex (i), which then dissociates to form a substituted phosphate (ii-a) and protonated 4E (ii-b). It has been reported that the protonated aromatic amines can be easily oxidized to form radical cations.^{17,18} In our case, ii-b was oxidized to form iii. The

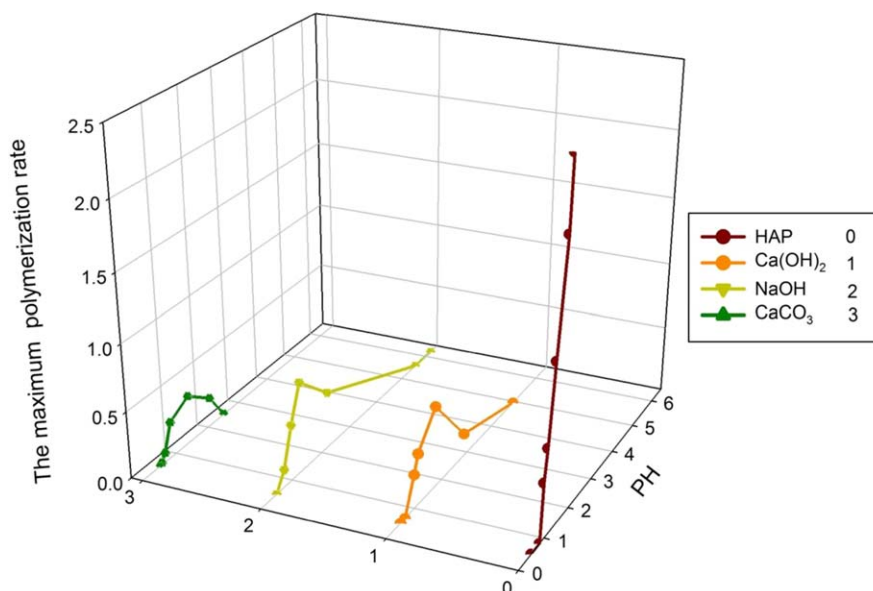


Figure 4. 3-D plot of R_p of the HEMA/2MP system with the addition of different bases varied from 0.5 to 8 wt % (4E content = 0.088 mmol/g, water content = 20 wt %). The x axis represents the category of the bases, the y axis is the initial pH of the adhesive system, and the z axis represents R_p of the 2MP/HEMA adhesive system. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

substituted phosphate (ii-a) then deprotonated the radical cation (iii) by the abstraction of one proton from the methyl group on iii to form the 4E free radical (iv). Thus, this free radical (iv) attacked the double bond on the 2MP/HEMA monomers to form the chain-initiating radicals; this was followed by chain propagation to form living polymers. In the meantime, these living polymers underwent the termination process to form a dead polymer by the combination of the coupling and disproportionation reaction. In the 2MP/HEMA adhesive system, the chain termination rate ($\frac{\partial c}{\partial t}$) was clearly diffusion-controlled and followed Fick's Law:¹⁹

$$\frac{\partial c}{\partial t} = D_0 \nabla C \quad (2)$$

where ∇C is concentration gradient, D_0 is the diffusion coefficient and is calculated as follows:

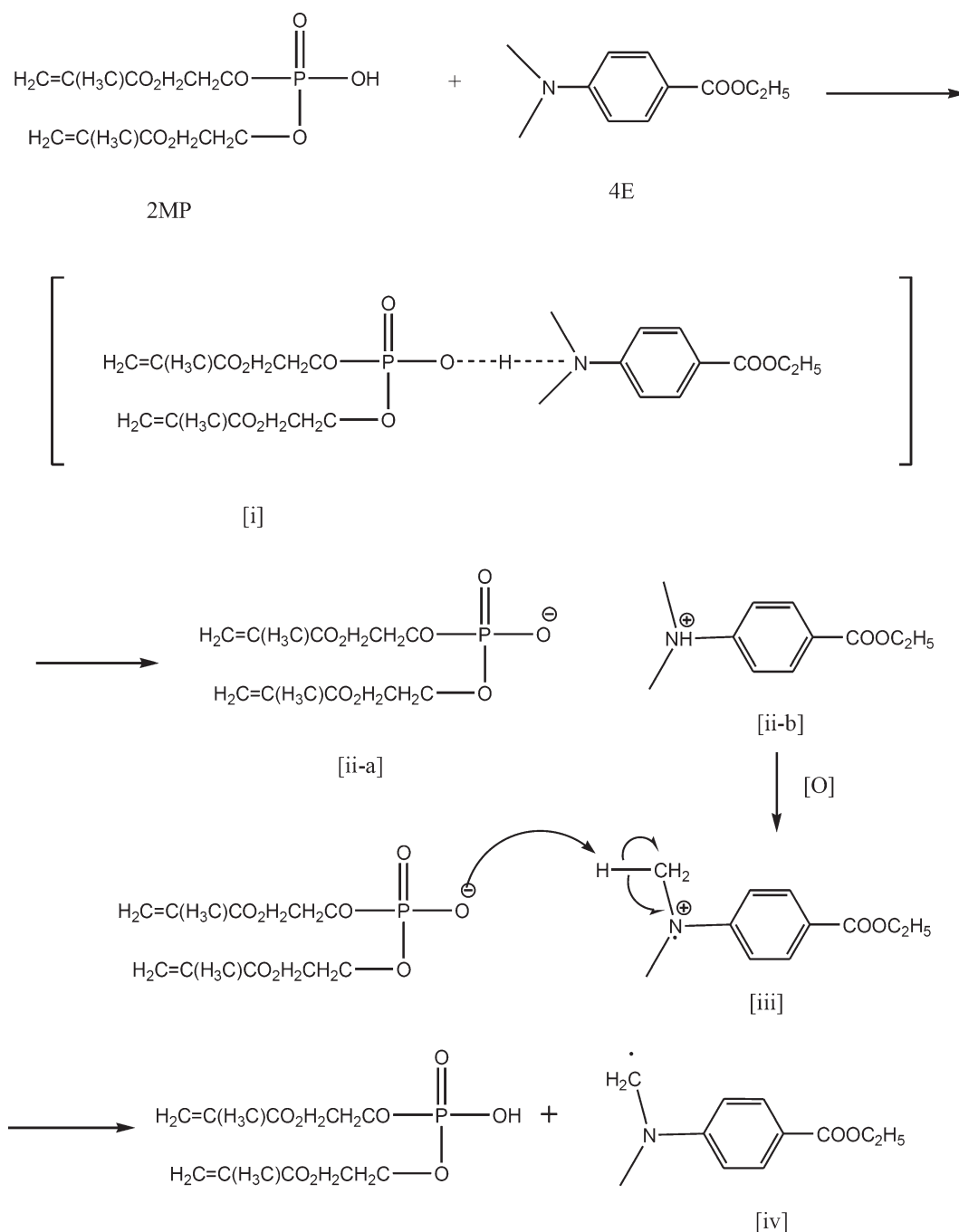
$$D_0 = \frac{\kappa_B T}{6\eta\pi r} \quad (3)$$

where κ_B is Boltzman constant, T is temperature, η is the viscosity of the system and r is the radius of the living polymer.

Initially, the diffusion coefficient was quite large because both the viscosity of the system and the radius of the living polymer were small. For a certain period (IP), polymerization was under its initial steady state; that is, the termination rate of the chain reaction was approximately same as the rate of initiation so that the polymerization rate was very low. As the reaction proceeded while the average radius of living polymer (r) and the viscosity of the system (η) built up to the threshold (right after IP), the polymerization rate increased remarkably because of the prompt decrease of the termination rate. When the bulk monomer was close to depletion or an inhibition reaction overcame the propagation process, the polymerization rate decreased.

At low pH (e.g., at pH = 0.50 before addition of base), because of the high proton concentration, the substituted phosphate (ii-a) was immediately converted to its acidic form (2MP), and thus, the concentration of the base form [the substituted phosphate (ii-a)] was too low to take protons from the methyl group on radical cations (iii; Scheme 1). As a result, there were not enough free radicals (iv) generated to build up the polymer size and viscosity. Thus, the threshold for bulk polymerization initiation could not be passed, and no reaction was observed. On the other hand, when the increase in pH for the adhesive system passed its optimum region [e.g., at pH 4.95 and with 8 wt % $\text{Ca}(\text{OH})_2$], most 2MPs are in their dissociated form, phosphate (ii-a); thus, there was not enough acid form of 2MPs to generate the complex (i). As a result, no spontaneous polymerization took place at high pH either. As a balance of both effects, 2MP in a suitable proportion of base form and acid form was required to generated free radicals (iv). So the optimum pH range was close to its pK_a of 1.70,²⁰ which perfectly matched our experimental results.

With regard to the second question of why such a dependency of the polymerization behavior on pH was not noticed before for systems similar to ours, we could find the answer in the proposed mechanism (Scheme 2) as well. Our aromatic amine (4E) was distinctively different from the aromatic amines that were reported^{13,14,21,22} to trigger the spontaneous polymerization without additional activators. That is, those amines [including NPG, *N*-*p*-tolyl glycine, and *N*-phenyl iminodiacetic acid (PIDDA)] all bore carboxylic acid functional groups themselves, whereas 4E did not. In other words, NPG, *N*-*p*-tolyl glycine, and PIDAA all existed in a zwitterion form; this ensured the supply of an amine radical cation precursor (e.g., ii-b in Scheme 2) and carboxylate nucleophile, both of which were crucial for the generation of free radicals. As a result, no additional activator was necessary. In contrast, 4E only had a tertiary amine group to

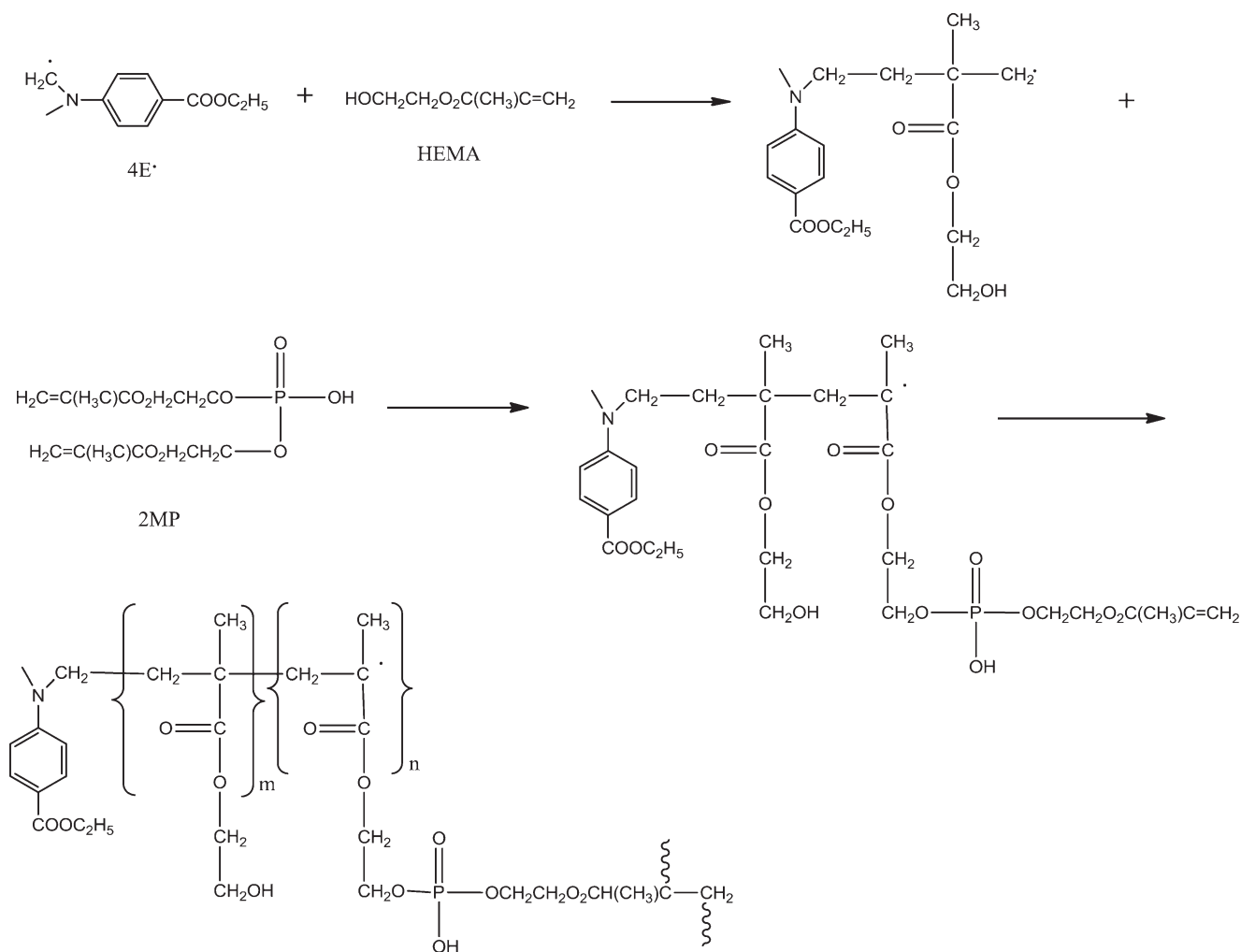


Scheme 1. Formation of 4E free radicals resulting from the decomposition of the acidic monomer 2MP/4E complex.

provide the amine radical cation and thus requires deprotonated 2MP to act as a nucleophile. As a result, bases had to be added to the acidic HEMA/2MP/4E adhesive system to adjust the pH to a range that was most favorable for the generation of both radical cations and the phosphate nucleophile.

Although all of the four bases investigated in this study could attenuate the acidity of the adhesive resin and render an almost complete DC as a result, HAP stood out as the most efficient activator, as evidenced by the fastest polymerization rate. As shown in Figure 4 and Table I, R_p of the HAP-activated system in the identified optimal pH range (1.0–1.8) was much higher

than the other three base-activated systems. The peak R_p of the HAP-activated system (2.4%/min with 8% HAP at pH 1.62) was more than four times that of the rest, and the induction time of this particular formulation was only 10 min, too. The extraordinary efficiency of HAP as an activator was due to its ability to form a phosphate-buffered system, whereas the other bases we studied could not. As the polymer size increased, the radical (iv) formation step during which a proton was excluded and the phosphate (ii-a) formation step may not have occurred simultaneously at the same location. Consequently, the subtle variation of the local proton concentration took place in the



Scheme 2. Polymerization of the HEMA/2MP monomers initiated with 4E free radicals.

HEMA/2MP/4E adhesive system. A higher buffer capacity mitigated the change in proton concentration in the local environment during the reaction process so that the polymerization process was less likely to be affected by this local pH variation. In other words, the buffer effect helped to maintain the pH at the optimal value throughout the entire solution and facilitated the chain propagation as a result.

Our discovered 4E-initiated polymerization in the presence of various bases showed distinct advantages over other aromatic amines, such as the NPG-initiated polymerization. As described previously, NPG was very active, and this could have led to spontaneous free-radical polymerization without an additional activator. Adhesives containing NPG would lead to unwanted, uncontrollable gelification (polymerization) of acrylic monomers,^{13,14} and the storage stability of these adhesives was significantly decreased. Thus, NPG was eliminated as a co-initiator in the CQ/amine photo-initiation system, especially for aqueous acidic adhesive formulations.²¹ In contrast, 4E was less active, and it is widely used as a co-initiator in the CQ/amine photo-initiation system.^{3,7,16} Our results indicate that the spontaneous polymerization with 4E initiation could be controlled by the

adjustment of pH and could be especially activated by HAP. 4E could potentially be used to activate polymerization through a dual-curing approach. This unique way of tooth-originated activation deserves further attention.

CONCLUSIONS

The 4E-initiated spontaneous polymerization of the 2MP/HEMA aqueous adhesive system in the presence of various bases was investigated. Our results reveal that the pH of the adhesive system was critical for this polymerization process. Therefore, for spontaneous polymerization, it was important to adjust the pH to a suitable range with appropriate activators, such as HAP. In addition the pH effect, the different type of activators (i.e., bases) resulted in a different buffer capacity of the HEMA/2MP/4E adhesive system; this also played an important role in the polymerization process. On the basis of the results, the optimum pH of this system was between 1.0 and 1.8, and HAP had the best effect on the polymerization because of its excellent buffer capacity. Future work is needed to verify whether polymerization will occur when the adhesive system is applied in a HAP-containing tooth substrate. It is also necessary to investigate the pH effect and 4E efficiency in other acidic

adhesive systems and the spontaneous polymerization of adhesives with the substitution of 4E with other amines as initiators.

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