Radical Annihilation of γ-Ray-Irradiated Contact Lens Blanks Made of a 2-Hydroxyethyl Methacrylate Copolymer at Elevated Temperatures

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ABSTRACT: The annihilation of the radicals in irradiated 2-hydroxyethyl methacrylate copolymer was analyzed by the use of electron paramagnetic resonance (EPR) spectroscopy. The EPR spectra were deconvoluted into three radicals: a quartet (Ra), a triplet (Rb), and a broad singlet (Rc). Radical Ra was attributed to coupling with a methyl radical and/or a doublet or triplet with about the same hyperfine coupling due to a methylene radical. Radical Rb was due to a methylene radical produced by main-chain scission. Radical Rc was attributed to various free radicals without coupling to protons. By comparing the EPR spectra of radicals Ra, Rb, and Rc with the spectrum of a 2,2-diphenyl-1-picrylhydrazyl (DPPH) standard with a known spin number, we calculated the spin numbers of the radicals, which decreased with time in the temperature range 25–45°C, regardless of the irradiation dose. The annealing of Ra and Rb and the annealing of Rc at longer times followed second-order kinetics; these were different from the kinetics for the color formation and defect-controlled hardening of polymers. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 117: 3114–3120, 2010

Key words: annealing; biomaterials; ESR/EPR; hydrophilic polymers; radiation

INTRODUCTION

2-Hydroxyethyl methacrylate (HEMA) copolymers and related hydrogels have been widely used as biocompatible materials, including soft contact lenses,[1,2] kidney dialysis systems,[3,4] artificial liver support systems,[5,6] and drug-delivery systems.[7,8] The structure of HEMA allows water contents similar to living tissues and is inactive to normal biological processes, resistant to degradation, unabsorbed by the body, permeable to metabolites, and able to be prepared in various shapes and forms. The HEMA copolymer consists of a hydroxyl group, which is hydrophilic, a methyl group, which supports the hydrolytic stability, and a carbonyl group, which is highly polarizable.[9–11]

When polymeric materials are subjected to γ-ray irradiation, the main effects are the scission of main chains and the creation of free radicals, double bonds, crosslinkages, end linkages, and so forth.[12,13] When main-chain scission, crosslinking, and/or end-linking occurs, the molecular size distribution and/or the structure is changed. These effects change the physical, chemical, and mechanical properties of polymeric materials. The free radicals and double bonds are able to absorb certain wavelengths of visible light and, thus, afford color centers.[14–17] The color center in irradiated polycarbonate has been attributed to substituted benzophenones,[18] radical species,[19,20] highly conjugated compounds,[21] and/or rearranged isopropylidene radicals.[22] The color center of the irradiated HEMA copolymer was also studied;[17] however, the origin of the color centers was not identified. Kudoh[23] reported that the mechanical properties of poly(methyl methacrylate) (PMMA) were degraded by γ-ray irradiation. Lu et al.[24] studied the evolution of the hardness of irradiated HEMA copolymer at elevated temperatures and found that the hardness increased with time during isothermal annealing; this was attributed to crosslinkage.

Radicals are one of the major products of polymeric materials irradiated with γ rays. These radicals can be studied effectively with electron paramagnetic resonance (EPR) spectroscopy.[25] Kuzuya et al.[26] studied the plasma-induced radicals of several crosslinked methacrylic polymers and found

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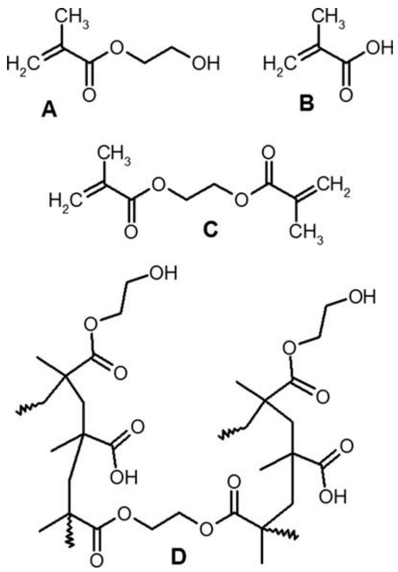

Figure 1 Chemical structures of (a) HEMA, (b) MAA, and (c) ethylene glycol dimethacrylate and (d) representation of the connection and crosslink in the copolymer.

that crosslinkage stabilized the radicals and suppressed polymer degradation. The EPR spectrum of irradiated poly(2-hydroxyethyl methacrylate) (PHEMA) was composed of a four-line component, a doublet, and a broad singlet, which were assigned to the chain scission of the methylene radical ($-\dot{C}H-$) and an immobilized dangling bond site.[26] This spectrum was observed by Hill et al.[27] at room temperature. However, the EPR spectrum obtained at 77 K was proposed to be composed of six types of radicals: $^{\cdot}CH_3$, $^{\cdot}CH_2CH_2OH$, $-COO\dot{C}HCH_2OH$, $^{\cdot}COO-$, $-\dot{C}H-$ and $^{\cdot}CHO$. The molecular structure of PHEMA is very similar to that of PMMA, which undergoes chain scissions upon γ-ray irradiation.[28] Moreover, the loss in transmittance during isothermal annealing and the evolution of hardness of irradiated HEMA copolymer has been further investigated. However, the correlations between the color centers and hardness with radicals have not yet been established. Recently, Silva et al.[29] studied the radical decay of different polypropylenes irradiated at 25 kGy at room temperature and proposed a mixed-order process (first and second orders) to explain the radical annihilation. This prompted us to investigate the kinetic aspects of irradiated HEMA copolymer at elevated temperatures by means of EPR spectroscopy with the aim of gaining a better understanding of the relationship between irradiation-generated free radicals and the physical and mechanical properties, such as hardness and color, with further application in the radiation sterilization of contact lenses.

EXPERIMENTAL

The soft contact lens blanks of HEMA copolymer were obtained from Canadian Contact lens

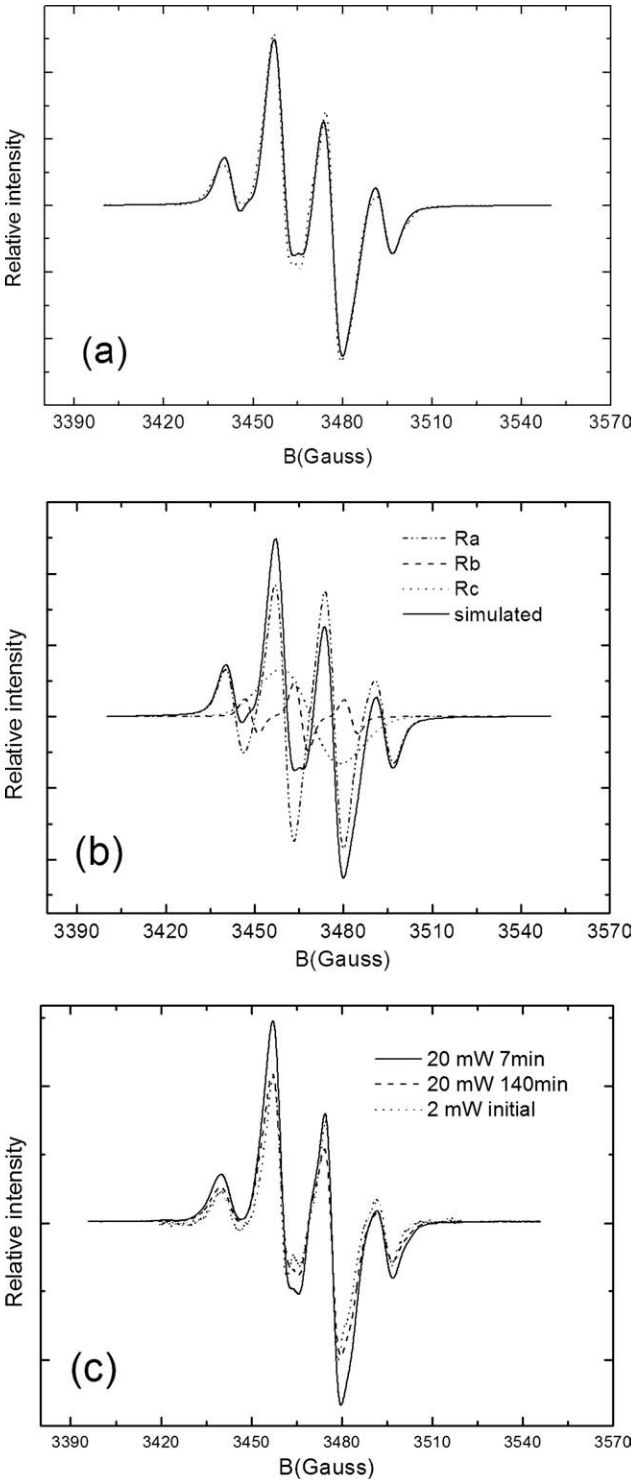

Figure 2 (a) EPR spectrum of HEMA irradiated with 320 kGy and annealed at 25°C for 15 min (• • •) and simulated spectrum (—) of three radicals. (b) Deconvoluted spectra of radicals Ra, Rb, and Rc and overall simulated spectrum. (c) EPR spectra of another sample at 20 mW with different annealing times after irradiation and spectrum of the sample at 2 mW right after irradiation at 25°C. B is the magnetic induction.

TABLE I
Isotropic EPR Parameters of the Radicals Obtained from the Deconvolution of the Spectrum of PHEMA (Fig. 2)

Radical	g factor	Pattern	Number of equivalent protons	Hyperfine coupling constant (G)	Peak-to-peak line width of the individual line (G)
Ra	2.0040 (2)	1 : 3 : 3 : 1	3	17 (2)	6
Rb	2.0056 (2)	1 : 2 : 1	2	17 (2)	4
Rc	2.0038 (2)	1	—	—	20

The numbers in parentheses are the estimated standard deviations.

Laboratories, Ltd. (Montreal, Canada). The copolymer consisted of HEMA, ethylene glycol dimethacrylate, and methacrylic acid; their schematic structures are shown in Figure 1. The specimens were cut from soft contact lens blanks 12.8 mm in diameter and 6 mm in thickness and ground to yield a sample about 2 × 2 × 2 mm^3. The specimens were ground with 600-, 800-, and 1200-grit emery papers. To eliminate the residual stresses, they were annealed *in vacuo* at 60°C for 48 h and then cooled to room temperature in a furnace.

The specimens were placed in glass tubes and sealed *in vacuo*. They were irradiated by a Co^{60} γ-ray source with a dose rate of 16 kGy/h at room temperature to afford doses of 320, 480, 640, and 800 kGy at the Radioisotope Division, National Tsing Hua University.

EPR spectra were recorded on a Bruker EMX-10 EPR spectrometer (Kahrsrule, Germany) with a dual cavity at 25°C. A typical spectrum was taken with a microwave power of 20.0 mW, a modulation amplitude of 4.0 G (the use of 0.8 G did not improve the resolution noticeably but significantly decreased the signal-to-noise ratio), a time constant of 20.5 ms, a sweep time of 168 s, and a scan range of 150 G. The EPR spectrum of each specimen was measured immediately after the completion of irradiation. The annealing temperatures were 25, 30, 35, 40, and 45°C, which were lower than the glass-transition temperatures (54 and 40°C with 0 and 800 kGy irradiation). When a specimen was measured with a one-cavity port, the corresponding EPR spectrum of the 2,2-diphenyl-1-picrylhydrazyl (DPPH) standard was measured under the same conditions used in the other port. The DPPH standard had a total spin of 2.0×10^{15}. The EPR spectra were resolved into several components with computer simulation by the use of the software WinSim 2002 (Houston, TX). We simulated the spectrum by increasing the number of components until a reasonable fit was obtained, in which the number of $S = \frac{1}{2}$ nuclei was manually fixed and the values of Lande g factor, coupling constants, and line widths were set as floating parameters until a reasonable fit was obtained. Upon double integration of the EPR signals and comparison with that of DPPH, the number of spins of the radical corresponding to each component was determined.

RESULTS AND DISCUSSION

The EPR spectra of the HEMA copolymer irradiated with the Co^{60} γ-ray source at doses of 320, 480, 640, and 800 kGy at room temperature were very similar to each other. Because radical density is supposed to be proportional to radiation dose, the results indicated that the generation and decay of the radicals reached equilibrium during the time period of the irradiation. The dashed trace in Figure 2(a) illustrates a typical EPR spectrum of the HEMA copolymer irradiated with 320 kGy and annealed at 25°C for 15 min. The spectrum could be deconvoluted into the three components shown in Figure 2(b). The parameters for the simulation of the deconvoluted components are listed in Table I. The quartetlike spectrum could not be fitted with only one quartet component nor could it be well fitted with two components of a quartet and a triplet, yet it was reasonably well fitted when a broad feature was added to the simulation. The four-line component (dubbed Ra) with an intensity ratio of 1 : 3 : 3 : 1 and a large hyperfine coupling of 17 G could be attributed to (1) a radical coupled with a methyl $-CH_3$ group and/or (2) a doublet or triplet with about the same hyperfine coupling due to a methylene radical $\dot{C}H_2-CH_2-$ that was coupled to a vicinal proton at an anti position. The hyperfine coupling of the methyl radical trapped in methane matrix at 4.2 K was previously determined to be 23.0 G,[30] which was significantly larger than the value herein. Thus, a free methyl radical was not a good candidate for Ra. A methyl group at the vicinal position to a radical can afford a coupling constant in a large range of 13–23 G, depending on the neighboring functional groups.[31,32] Because all the three monomers in the copolymer contained the methyl group [Fig. 1(D)], main-chain cleavage of the copolymer could generate radicals adjacent to a methyl group, such as the cleavage at the $(CH_3)C_\alpha$–carboxyl bond to yield a $(CH_3)C_\alpha$· radical moiety. The intensity of radical Ra was the highest among the three radicals; this suggested that the main chain was the predominant site for radiolytic cleavage under the experimental conditions. In the case of the methylene radical, however, the free rotation along the methylene bond may have rendered the vicinal coupling to be averaged out and became smaller and unresolved, which would have afforded a triplet signal.

The radical of three lines with an intensity ratio of 1 : 2 : 1 (dubbed Rb) could have been due to a methylene radical produced via main-chain scission, as discussed previously. The broad singlet, dubbed Rc, may have been due to various free radicals without coupling to protons, such as a carboxylate radicals after breakage of the main chain and tertiary radicals after the cleavage of the methyl group. Extensive cleavage of the side chains may have generated tertiary radicals on the main chain in close proximity, which could have afforded a broad feature because of magnetic coupling among the radicals. The sum of the spectra of Ra, Rb, and Rc [solid trace in Fig. 2(a)] was in good agreement with the experimental data (dashed trace). A different sample showed virtually the same spectral features as this one [Fig. 2(c)], confirmed the formation of the radicals, and showed that the sample after a longer annealing time of 140 min or acquired at a lower microwave power of 2 mW afforded a lower signal intensity. The use of the high power of 20 mW increased the signal intensity by about 200% for clear detection of signal decay and 32% saturation relative to that with 2.0 mW [cf. Fig. 2(c)], which resulted in an overestimate of the rate constant *a* that could be calibrated. However, the reaction order and activation energy (from the slope of log *a* versus $1/T$ plots) were not affected, where T is Kelvin temperature.

The double integral of each spectral component is proportional to the product of signal height (H) and the square of the peak-to-peak width (ΔH) of its derivative spectrum ($H \times \Delta H^2$), where H is the magnetic field intensity. Therefore, by comparing the double integral of a spectral component with that of DPPH standard, one can obtain the number of spin of the corresponding radical. The spin concentration of the HEMA copolymer was equal to the total number of spin divided by the volume of 8 mm^3. The spin concentrations of radicals Ra, Rb, and Rc in specimen irradiated with 480 kGy as a function of time at different temperatures are shown in Figure 3(a–c), respectively. The initial time in Figure 3(a–c) occurred when the specimen was placed in the cavity port of the EPR spectrometer. That is, the period (ca. 15 min) of the specimen taken from the γ-ray source to the EPR spectrometer did not count in Figure 3(a–c). Similar decays of the spin concentrations of Ra, Rb, and Rc in the specimens irradiated with doses of 320, 640, and 800 kGy were observed. Herein, the concentrations, N, of the radicals decreased with increasing annealing time in all cases. Furthermore, the spin concentrations of radicals Ra and Rb followed a second-order annihilation process with annealing time, t, that is

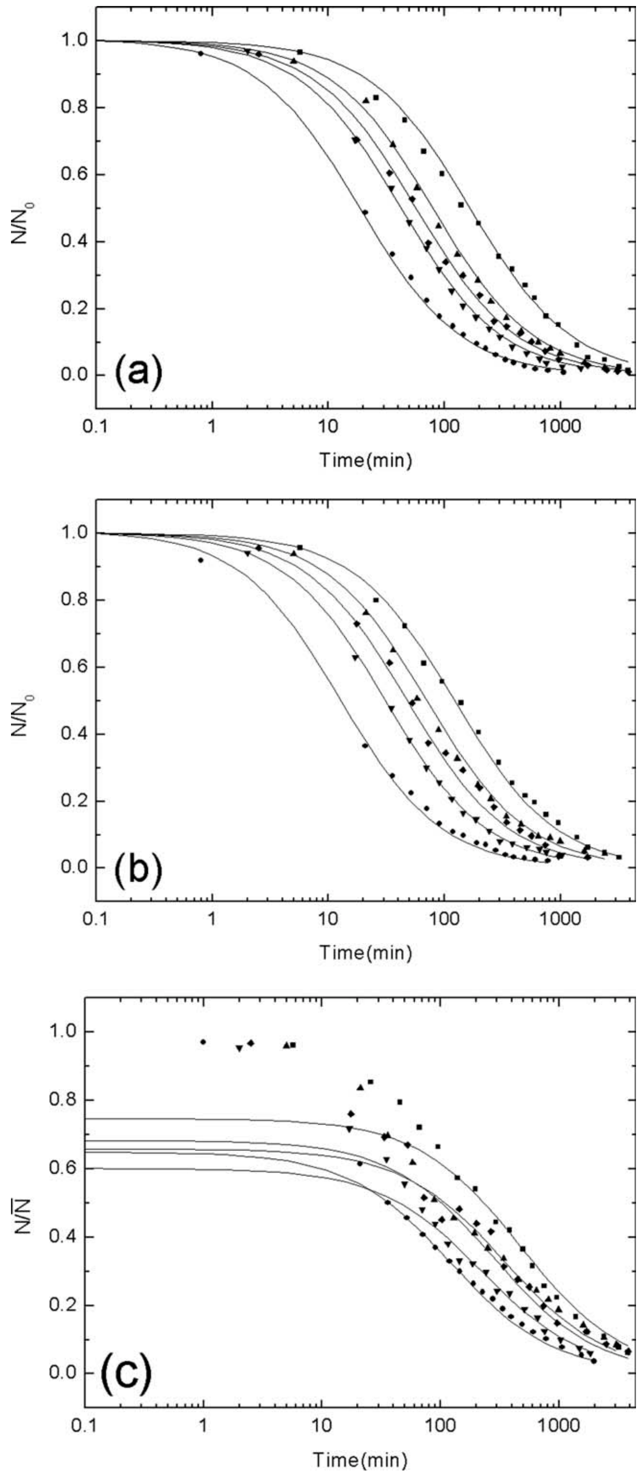

Figure 3 Time-dependent spin densities of (a) Ra, (b) Rb, and (c) Rc in specimens irradiated with 480 kGy at (●) 25, (▼) 30, (◆) 35, (▲) 40, and (■) 45°C.

$$\frac{dN}{dt} = -aN^2 \qquad (1)$$

where *a* is the rate constant that indicates the reaction between two radicals. Equation (1) could be solved as eq. (2):

TABLE II
N_0 Values of Radicals Ra, Rb, and Rc of the HEMA Copolymer and N Values of Radical Rc (Fig. 3)

Irradiation dose (kGy)	Temperature (°C)	N_0		
		Ra ($\times 10^{16}$)	Rb ($\times 10^{15}$)	Rc ($\times 10^{16}$)
320	25	4.8	3.7	3.0 (3.70)
	30	3.45	3.0	2.1 (2.75)
	35	5.15	4.0	3.2 (3.90)
	40	4.25	3.3	2.2 (3.80)
	45	4.6	3.4	2.0 (3.50)
480	25	4.3	4.1	2.7 (3.55)
	30	3.95	4.0	2.4 (3.65)
	35	4.4	4.2	2.3 (3.30)
	40	2.8	2.6	1.5 (2.50)
	45	4.5	4.4	2.2 (3.40)
640	25	2.45	2.3	1.8 (2.30)
	30	3.6	3.7	3.1 (4.20)
	35	4.5	4.9	2.5 (3.40)
	40	3.3	3.6	2.4 (3.65)
	45	4.3	4.6	2.0 (3.30)
800	25	2.9	2.5	2.2 (2.80)
	30	2.2	2.1	1.8 (2.75)
	35	2.7	2.6	1.6 (2.60)
	40	3.4	3.2	2.1 (3.80)
	45	4.3	4.2	1.1 (4.40)

$\overline{N}$ values are shown in parentheses.

$$\frac{1}{N} = \frac{1}{N_0} + at \tag{2}$$

where N_0 is the initial concentration. The solid traces in Figure 3(a,b) are the fitted results according to eq. (2), from which N_0 was obtained (listed in Table II). The rate constant as a function of the temperature satisfied the Arrhenius equation [see Fig. 4(a,b)], which afforded the activation energy listed in Table III. When the irradiation dose was in the range 320–800 kGy, the activation energy was 34 kJ/mol for radical Ra and 33–39 kJ/mol for radical Rb.

The annealing of radical Rc at short times was complicated. This was probably because this radical was not a chain-scission radical and was composed of various radicals, as discussed previously, which all annealed simultaneously to afford a complicated annealing pattern. A similar phenomenon was observed in a polypropylene blend radiated at 25 kGy.[29] Because of the complicated compositions and low radiation dose, the radical concentrations decreased to a minimum and then increased with increasing time until they reached a constant value. The process consisted of the generation and annihilation at the zero and first orders. Therefore, the authors only analyzed the finite time before radical regeneration. In the study herein, kinetics of radical Rc was considered at longer times. At longer times, the spin concentration of radical Rc followed second-order annihilation kinetics. The solid traces in Figure 3(c) were fitted to results based on eq. (2) for the longer times, wherein the rate constants as a function of the temperature are shown in Figure 4(c). The concentration in Figure 3(c) is the normalized concentration ($\overline{N}$), which was different from N_0 to fit eq. (2). The N_0 and $\overline{N}$ values are listed in Table II. Again, the rate constant of radical Rc increased

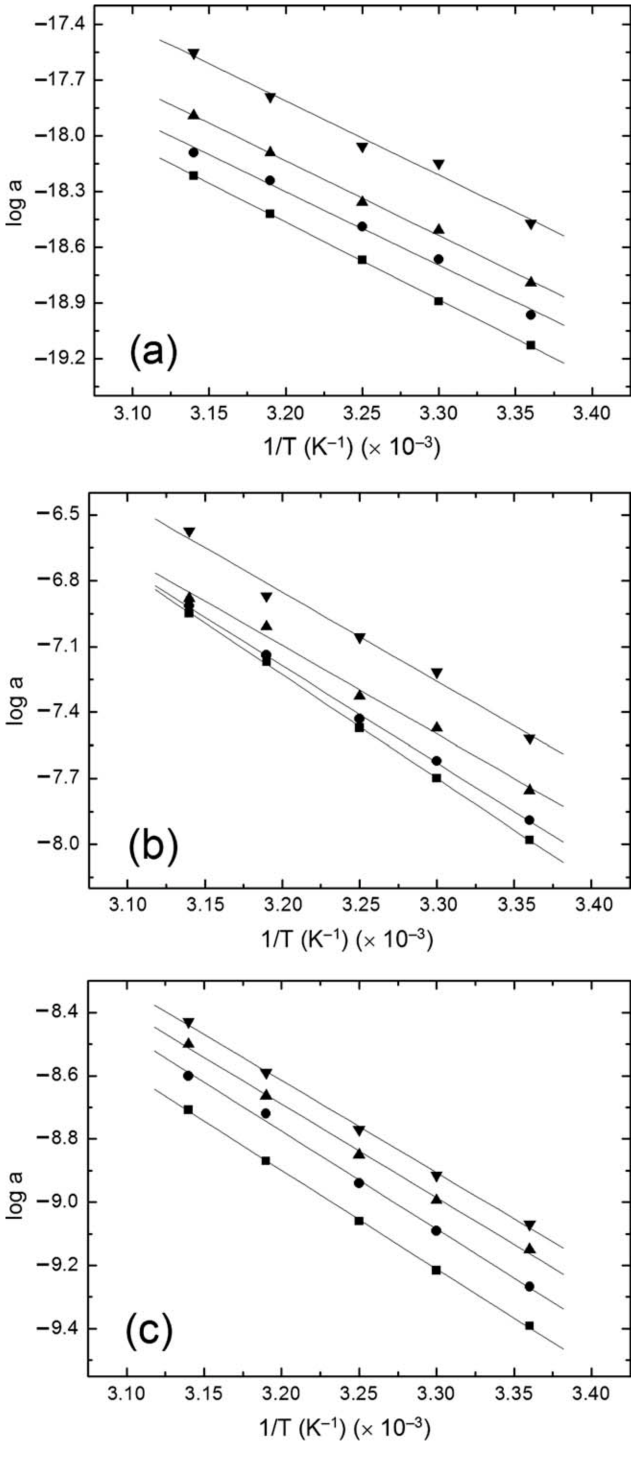

Figure 4 Arrhenius plots for the rate constants of the annealing process of (a) Ra, (b) Rb, and (c) Rc at (■) 320, (●) 480, (▲) 640, and (▼) 800 kGy.

TABLE III
Activation Energies (kJ/mol) of Radicals Ra, Rb, and Rc of HEMA

	Activation energy (kJ/mol)			
Radical	320 kGy	480 kGy	640 kGy	800 kGy
Ra	34.7 ± 0.3	34.3 ± 1.9	34.9 ± 1.6	34.6 ± 2.8
Rb	33.7 ± 2.2	33.5 ± 1.8	36.7 ± 0.8	39.1 ± 0.4
Rc	24.2 ± 0.5	24.6 ± 0.6	25.7 ± 0.8	25.9 ± 0.2

with increasing temperature, following the Arrhenius equation to afford activation energies in the range 24–25 kJ/mol irradiated with doses of 320–800 kGy. The activation energy of Rc at a given dose is smaller than those of Ra and Rb (which are similar within error), suggesting different natures of the two groups of radicals. The activation energy for Rc was possibly associated with an ensemble of isolated spins, representing the average thermodynamic and kinetic processes of Rc. The energy barriers of reaction for each radical at all doses were pretty much the same within the error range.

The transmission in the ultraviolet–visible spectra of a HEMA copolymer irradiated under the same conditions herein was found to decrease with elevated temperatures.[17] The transmission loss was attributed to the generation of color centers by the irradiation, which increased with increasing annealing time. The color center generation followed a first-order kinetic process. However, the annealing of the radicals was based on a second-order kinetic process, as shown in the studies herein. The different kinetic orders implied that mechanism for the formation of the color centers was different from the annihilation of radicals Ra, Rb, and Rc. Thus, the color centers arising directly from the radical could be ruled out. The color centers should have been correlated to certain degrees for the formation of chromophores via proton extraction and double-bond formation. The isothermal annealing of the hardness of a HEMA copolymer irradiated under the same conditions herein was also investigated,[24] wherein the hardness was contributed by some defects in the polymer caused by the irradiation. The defects that controlled the hardness increased with increasing annealing time and followed a first-order kinetic process that was different from that of the radical annealing we observed herein. Thus, the annealing processes of radicals Ra, Rb, and Rc observed herein did not seem to be attributable to the defect-controlled hardness.

CONCLUSIONS

The annealing kinetics of an irradiated HEMA copolymer at elevated temperatures was investigated with EPR spectroscopy. After irradiation of the copolymer with γ rays ranging from 320 to 800 kGy, the radicals generated were measured with an EPR spectrometer. The EPR spectra were deconvoluted into three components of three different types of radicals Ra, a quartet; Rb, a triplet; and Rc, a broad singlet. Radical Ra was most likely to be attributable to a radical coupled with a methyl radical, although it might have been due to a doublet or triplet with about the same hyperfine coupling due to a methylene radical. Radical Rb was due to a methylene radical produced by main-chain scission. Radical Rc was attributed to various free radicals without significant coupling to protons. For a given dose and temperature, the spin concentration of each radical decreased with time. The annihilation process of radicals Ra and Rb and radical Rc at longer times followed second-order kinetics. For all radical decays, the rate constant satisfied the Arrhenius equation, with activation energies of 35.1, 37.1, and 26.5 kJ/mol on average for radicals Ra, Rb, and Rc, respectively, at various radiation doses. Both the color centers related to irradiated PMMA[17] and defect-controlled hardness[24] followed a first-order kinetic process. These observations imply that the latter cases were not mainly attributed to the radicals Ra, Rb, and Rc resolved herein.

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