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RADICAL POLYMERIZATION OF METHYL METHACRYLATE INITIATED WITH POTASSIUM PERSULFATE IN THE PRESENCE OF NUCLEIC ACID BASE OR BENZO[a]PYRENE†

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It was found that nucleic acid bases and nucleosides could retard the radical polymerization of methyl methacrylate(MMA) initiated with $K_2S_2O_8$ in water. This chain transfer reaction may be the hydrogen abstraction from NH group or the addition of propagating chain radical onto C=C double bond. Also 5-fluorouracil, an antitumor drug, reacted effectively with propagating radicals to retard the polymerization. On the contrary, benzo[a]pyrene, which is known as a carcinogen, was found to promote strongly the radical polymerization of MMA in water.

Since 1962,$^{1)}$ we have been studying on the "uncatalyzed polymerization". One of the objects of the study is to observe the generation of free radicals in living organs by the reaction of vital macromolecule with vinyl monomer. Already we have reported that synthesized polyvinylphosphonate,$^{2)}$ enzymes, such as α-amylase$^{3)}$ and lysozyme,$^{4)}$ RNA,$^{5)}$ and vital cell of Saccharomyces cerviae$^{6)}$ could initiate the radical polymerization of methyl methacrylate(MMA) in aqueous phase.

The relationship between cancer disease and free radical has been discussed in the literature.$^{7)}$ The cancer disease may be a problem with respect to DNA. For example, the active center of the antibiotic bleomycin is considered to be located in the DNA-binding region.$^{8)}$ We are interested in these discussions, because the uncatalyzed polymerization can generate free-radicals in living organs.

The present paper concerns with the reactions of nucleic acid bases, 5-fluorouracil, an antitumor drug, and nucleosides with the propagating radical-chain of poly-MMA. Also this paper treats the promotion reaction with benzo[a]pyrene, a carcinogen, in the radical polymerization of MMA.

Experimental

Materials

Commercially available adenine(A), uracil(U), thymine(T), uridine(Ud), thymidine (Td), benzo[a]pyrene, benzo[a]anthracene, and anthracene were used without further purification. Imidazole(Im) and its derivatives were afforded by Shikoku Kasei Ind. Co.* and 5-fluorouracil(5-Fu) by Kyowa Hakko Co.* MMA and acrylonitrile(AN) were purified by the usual method. Water was ion-exchanged and distilled.

Procedures

Three cm^3 of MMA, a certain weight of additive and $1.5\mathrm{x}10^3$g of $K_2S_2O_8$ dissolved in 10 cm^3 of water were placed in a tube. After thawing with nitrogen, the tube was sealed under vacuum, and warmed at 60°C under shaking. After the reaction, the contents were poured into a large amount of methanol to precipitate the polymer. The conversion of MMA was calculated from the weight of the polymer so obtained.

The number average degree of polymerization ($\bar{P}_n$) of poly-MMA was estimated from $[\eta]$, measured at 30°C in benzene, according to Welch's equation.9)

Results and Discussion

1. Retardation of Radical Polymerization by Nucleic Acid Bases and Nucleosides

1.1 Time-Conversion Curves of Polymerizations of MMA

Figure 1 shows the retarding effects of uracil, thymine and uridine. A very small amount of pyrimidine base could retard the rate of polymerization of MMA up to about a half of the non-retarded rate. The retarding effects of uracil and uridine on the conversion of MMA were almost the same. Accordingly, it could be concluded that the center of retardation was not ribose but uracil itself.

1.2 Effect of the Concentration of Additives on the Polymerization of MMA

The conversion of MMA by the radical polymerization in an aqueous phase decreased with increase in the concentration of nucleic acid base, as shown in Fig. 2.

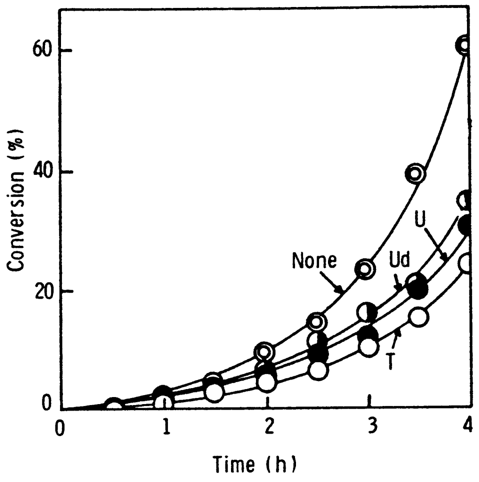


Fig. 1. Time-conversion curves of the polymerizations of MMA in the absence and presence of U, T or Ud. MMA 3 cm^3, $K_2S_2O_8$ 0.0015g, H_2O 10 cm^3; 60°C. $[U]=[T]=[Ud]=1.4 \mathrm{x} 10^{-2}$mol dm^3 with respect to the water phase.

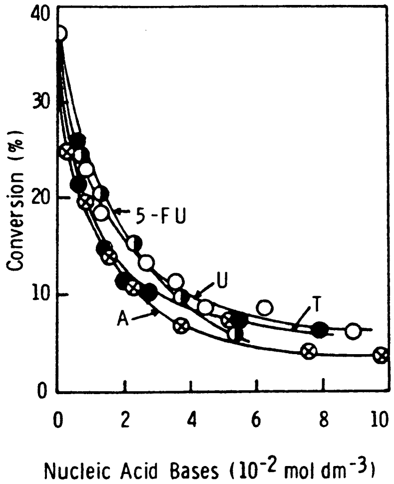


Fig. 2. Conversion of MMA vs. [A], [U], [T] or [5-FU]. MMA 3 cm^3, $K_2S_2O_8$ 0.0015g, H_2O 10 cm^3; 60°C, 3.5 h.

Interestingly, it was found that $\bar{P}_n$ of poly-MMA decreased monotonously with the concentration of the nucleic acid base.

The relationship between $\bar{P}_n$ and the concentration of the base was applied to the following Mayo's equation:11)

$$\frac{1}{\bar{P}_n} = \frac{1}{\bar{P}_{no}} + C_B\frac{[Base]}{[MMA]}$$

where $\bar{P}_{no}$ and $\bar{C}_B$ are $\bar{P}_n$ of poly-MMA produced in the absence of the base and the chain transfer constant of the propagating chain to the base, respectively.

It can be reasonably considered that the polymerization proceeds in aqueous phase and the [MMA] is constant at 1.6 g dm^{-3}, that is, 1.6 x 10^{-2}mol dm^{-3}.[10)]

As can be seen in Fig. 3, it was found that $\bar{P}_n^{-1}$ of the poly-MMA correlated linearly with the concentrations of uracil, adenine and 5-FU. The values of C_B were calculated to be 7.5 x 10^{-5}(adenine), 5.9 x 10^{-5}(uracil) and 3.03 x 10^{-5}(5-FU), respectively.

The examples for the retardation by nucleoside are shown in Fig. 4.

1.3 Retardation of Polymerization of MMA by Imidazole and its Derivatives

Figure 5 showed the results.

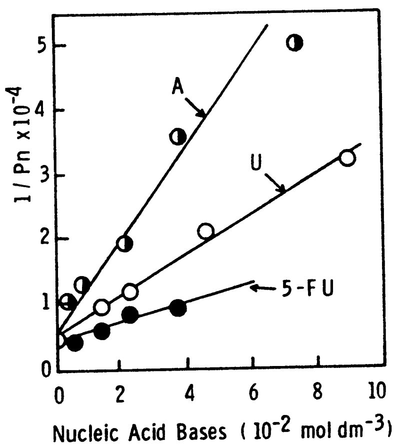


Fig. 3. $\bar{P}_n^{-1}$ of poly-MMA vs. [U], [A] or [5-FU]. MMA 3 cm^3, $K_2S_2O_8$ 0.0015g, H_2O 10 cm^3; 60°C, 3.5 h.

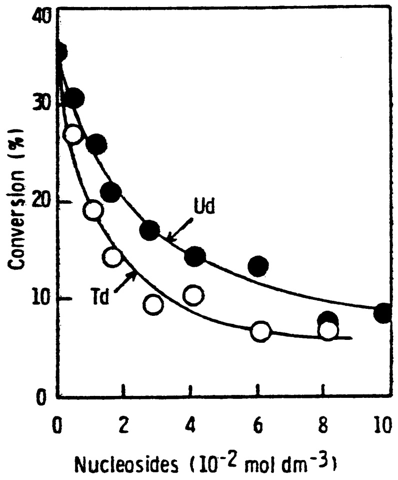


Fig. 4. Conversion of MMA vs. [Ud] or [Td]. MMA 3 cm^3, $K_2S_2O_8$ 0.0015g, H_2O 10 cm^3; 60°C, 3.5 h.

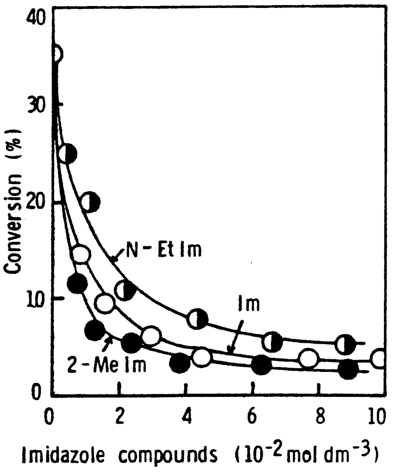
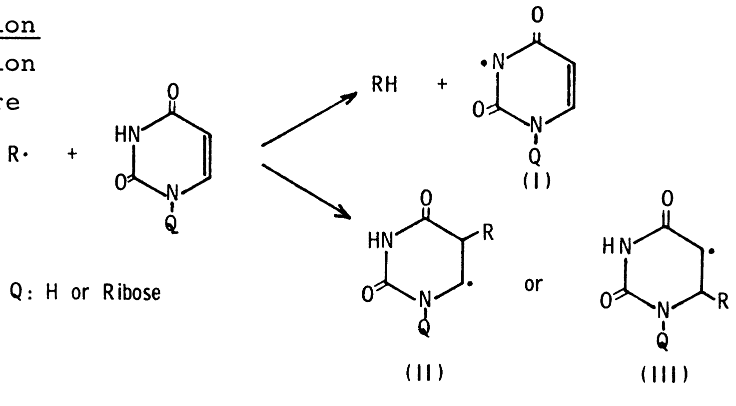


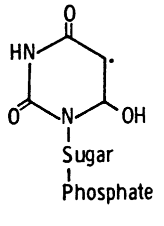
Fig. 5. Conversion of MMA vs. [Im's]. MMA 3 cm^3, $K_2S_2O_8$ 0.0015g, H_2O 10 cm^3; 60°C, 3.5 h.

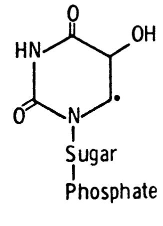
1.4 Assumed Mechanism of Retardation

As mentioned above, the retardation activities of uracil and uridine were almost the same. Accordingly, it was concluded that the chain transfer of the propagating radical to uracil or uridine occured in pyrimidine region. Thus, the mechanism of tha chain transfer reaction may be considered in the following two ways:



According to Hatano et al.,[12)] uridine monophosphate could add ·OH to its C=C bond by γ-irradiation in water, and the structures of the generated radicals were concluded to be as (IV) and (V) by the spin-trapping method. Hatano's results support the above mechanism.


(IV)


(V)

In the case of adenine, both the regions of pyrimidine and imidazol may be active.

2. Promotion of Radical Polymerization by Benzo[a]pyrene and Benzo[a]anthracene

Because benzo[a]pyrene is one of the typical carcinogenic compounds, we are interested in its effect on the radical reaction. The results obtained in the polymerization of MMA initiated with $K_2S_2O_8$ in an aqueous phase was worthy of astonishment, as shown in Fig. 6. As the conversion of MMA increased, $\bar{P}_n$ of poly-MMA increased. Benzo[a]pyrene is practically insoluble in water. However, a remarkable increase in conversion and $\bar{P}_n$ were observed. At the present time, we can not explain the results.

Also, benzo[a]anthracene showed a strong promotion effect and anthracene a weak one. The effects are shown in Fig. 7.

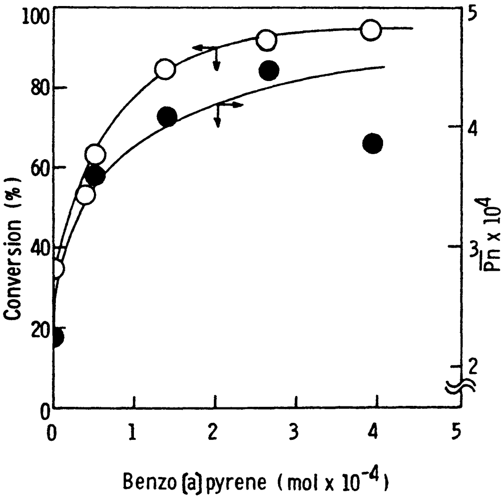


Fig. 6. Conversion of MMA vs. mass of benzo[a]pyrene. MMA 3 cm^3, $K_2S_2O_8$ 0.0015g, H_2O 10 cm^3; 60°C, 3.5 h.

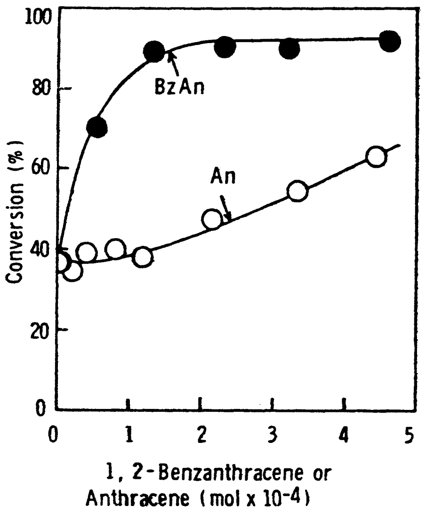


Fig. 7. Conversion of MMA vs. mass of benzo[a]anthracene or anthracene. MMA 3cm^3, $K_2S_2O_8$ 0.0015g, H_2O 10 cm^3; 60°C, 3.5 h.

References

1) S. Kimura, T. Takitani, and M. Imoto, Bull. Chem. Soc. Jpn., 35, 2012(1962). 2) M. Imoto, M. Sakae, and T. Ouchi, Makromol. Chem., in press. 3) M. Imoto, N. Sakade, and T. Ouchi, J. Polym. Sci., Polym. Chem. Ed., 15, 499(1977). 4) T. Ouchi, T. Yoshikawa, and M. Imoto, J. Macromol. Sci. Chem. A12, 1523(1978). 5) M. Imoto, Y. Nishida, T. Yoshikawa, and T. Ouchi, Bull. Chem. Soc. Jpn., 51, 1456 (1978). 6) M. Imoto, T. Ouchi, Y. Nakamura, T. Yamada, Y. Tokuyama, H. Obata, and T. Iwamoto, J. Polym. Sci. Polym. Lett. Ed. in press. 7) Chem. and Eng. News, 53 (30), 16(1975). 8) H. Umezawa, Kagakukyoiku, 26, 439(1978). 9) F. J. Welch J. Polym. Sci., 61, 243(1962). 10) The solubility of MMA in water is 1.5 g dm^{-3} at 50°C: M. Imoto, K. Ree, and T. Ouchi, Chem. Lett. 1973, 447. 11) F. R. Mayo, J. Am. Chem. Soc., 65, 2324(1948). 12) S. Kominami, S. Rokushika, and H. Hatano, Int. J. Radiat, Biol., 30, 525(1976); Radiat, Res., 72, 89(1977). 13) S. Takeuchi, M. Kochi, K. Sakaguchi, K. Nakagawa, and T. Mizutani, Agric. Biol. Chem., 42, 1449 (1978). 14) P. H. Burleigh, J. Am. Chem. Soc., 82, 749(1960): M. Imoto, K. Takemoto, and T. Nakai, Makromol. Chem., 48, 80(1961). †Vinyl Polymerization. 389.

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